

CERTIFICATE

I hereby certify that the annexed is a true copy of the Specification as filed on
18 February 2000 for International Patent application number PCT/NZ00/00015 made by
GENESIS RESEARCH AND DEVELOPMENT CORPORATION LIMITED.

Dated 8 March 2004.



Neville Harris
Commissioner of Patents, Trade Marks and Designs



PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

PCT/NZ00/ 00015

International Filing Date

18 FEB 2000 (18/02/2000)

NEW ZEALAND PATENT OFFICE P.C.T INTERNATIONAL APPLICATION

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference

(if desired) (12 characters maximum)

25562 MRB

Box No. I TITLE OF INVENTION

COMPOSITIONS ISOLATED FROM STROMAL CELLS AND METHODS FOR THEIR USE

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

GENESIS RESEARCH & DEVELOPMENT CORPORATION
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☐ This person is also inventor.

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This person is applicant for the purposes of:

☐ all designated States

☒ all designated States except the United States of America

☐ the United States of America only

☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

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This person is:

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☐ all designated States except the United States of America

☒ the United States of America only

☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒ agent

☐ common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

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If none of the following sub-boxes is used, this sheet should not be included in the request.

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This person is applicant for the purposes of:

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Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

KUMBLE, Krishanand D
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This person is:

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State (that is, country) of residence:

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This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☒ the United States of America only☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

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Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

MURISON, James Greg
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This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

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State (that is, country) of residence:

NZ

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

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This person is applicant for the purposes of:

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Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

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Box No.V DESIGNATION OF STATES

following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes: at least one must be marked):

Regional Patent

- ☒ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | |
|---|---|
| <input checked="" type="checkbox"/> AE United Arab Emirates | <input checked="" type="checkbox"/> LR Liberia |
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LS Lesotho |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LT Lithuania |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> MA Morocco |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BR Brazil | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CR Costa Rica | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> DM Dominica | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input checked="" type="checkbox"/> GD Grenada | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GH Ghana | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> GM Gambia | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> HR Croatia | <input checked="" type="checkbox"/> TZ United Republic of Tanzania |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> ID Indonesia | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> IN India | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> IS Iceland | <input checked="" type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> YU Yugoslavia |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> ZA South Africa |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> ZW Zimbabwe |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | |
| <input checked="" type="checkbox"/> KR Republic of Korea | |
| <input checked="" type="checkbox"/> KZ Kazakhstan | |
| <input checked="" type="checkbox"/> LC Saint Lucia | |
| <input checked="" type="checkbox"/> LK Sri Lanka | |

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

- ☐
- ☐

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

Box No. VI PRIORITY CLAIM		<input type="checkbox"/> Further priority claims are indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application: regional Office	international application: receiving Office
item (1) 25 March 1999 (25/3/1999)	09/276,268	USA		
item (2) 26 August 1999 (26/8/1999)	09/383,586	USA		
item (3)				

☐ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s):

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year)

Number

Country (or regional Office)

ISA / APO

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 5
description (excluding sequence listing part) : 25
claims : 3
abstract : 1
drawings : -
sequence listing part of description : 40

Total number of sheets : 74

This international application is accompanied by the item(s) marked below:

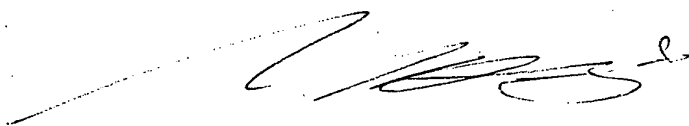
- ☒ fee calculation sheet
- ☐ separate signed power of attorney
- ☐ copy of general power of attorney; reference number, if any:
- ☐ statement explaining lack of signature
- ☐ priority document(s) identified in Box No. VI as item(s):
- ☐ translation of international application into (language):
- ☐ separate indications concerning deposited microorganism or other biological material
- ☒ nucleotide and/or amino acid sequence listing in computer readable form
- ☐ other (specify):

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).



MICHAEL ROY BENNETT
Agent for the Applicants

For receiving Office use only		For International Bureau use only	
1. Date of actual receipt of the purported international application:	18 FEB 2000 (18/02/2000)	2. Drawings:	
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		<input type="checkbox"/> received:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):		<input type="checkbox"/> not received:	
5. International Searching Authority (if two or more are competent): ISA / AU		6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.	

Date of receipt of the record copy by the International Bureau:

COMPOSITIONS ISOLATED FROM STROMAL CELLS AND METHODS FOR THEIR USE

10 Technical Field of the Invention

This invention relates to genes encoding proteins expressed in lymph node stromal cells from flaky skin (*fsn* $-/-$) mice and their use in therapeutic methods.

Background of the Invention

15 Lymph vessels and nodes are important components of the body's immune system. Lymph nodes are small lymphatic organs that are located in the path of lymph vessels. Large molecules and cells, including foreign substances, enter into the lymphatic vessels and, in circulating through these vessels, pass through the lymph nodes. Here, any foreign substances are concentrated and exposed to lymphocytes. This triggers a cascade of events that constitute
20 an immune response, protecting the body from infection and from cancer.

Lymph nodes are surrounded by a dense connective tissue network that forms a supporting capsule. This network extends into the body of the lymph node, forming an additional framework of support. Throughout the remainder of the organ, a fine meshwork can be identified that comprises reticular fibres and the reticular cells that produce and surround the
25 fibres. These features provide a support for the main functional cells of the lymphatic system, which are T- and B-lymphocytes. Additional cell types found in lymph nodes include macrophages, follicular dendritic cells, and endothelial cells that line the blood vessels servicing the node.

The cells within lymph nodes communicate with each other in order to defend the body
30 against foreign substances. When a foreign substance, or antigen, is present, it is detected by macrophages and follicular dendritic cells that take up and process the antigen, and display parts of it on their cell surface. These cell surface antigens are then presented to T- and B-lymphocytes, causing them to proliferate and differentiate into activated T-lymphocytes and plasma cells, respectively. These cells are released into the circulation in order to seek out and
35 destroy antigen. Some T- and B-lymphocytes will also differentiate into memory cells. Should these cells come across the same antigen at a later date, the immune response will be more rapid.

5 Once activated T- and B-lymphocytes are released into the circulation, they can perform a variety of functions that leads to the eventual destruction of antigen. Activated T-lymphocytes can differentiate into cytotoxic lymphocytes (also known as killer T-cells) which recognise other cells that have foreign antigens on their surface and kill the cell by causing them to lyse. Activated T-lymphocytes can also differentiate into helper T-cells which will then secrete
10 proteins in order to stimulate B-lymphocytes, and other T-lymphocytes, to respond to antigens. In addition, activated T-lymphocytes can differentiate into suppressor T-cells which secrete factors that suppress the activity of B-lymphocytes. Activated B-lymphocytes differentiate into plasma cells, which synthesise and secrete antibodies that bind to foreign antigens. The antibody-antigen complex is then detected and destroyed by macrophages, or by a group of
15 blood constituents known as complement.

 Lymph nodes can be dissociated and the resulting cells grown in culture. Cells that adhere to the tissue culture dishes can be maintained for some length of time and are known as stromal cells. The cultured cells are a heterogeneous population and can be made up of most cells residing within lymph nodes, such as reticular cells, follicular dendritic cells, macrophages
20 and endothelial cells. It is well known that bone marrow stromal cells play a critical role in homing, growth and differentiation of hematopoietic progenitor cells. Proteins produced by stromal cells are necessary for the maintenance of plasma cells *in vitro*. Furthermore, stromal cells are known to secrete factors and present membrane-bound receptors that are necessary for the survival of lymphoma cells.

25 An autosomal recessive mutation, designated flaky skin (*fsn* *-/-*), has been described in the inbred A/J mouse strain (The Jackson Laboratory, Bar Harbour, ME). The mice have a skin disorder similar to psoriasis in humans. Psoriasis is a common disease affecting 2% of the population, which is characterised by a chronic inflammation associated with thickening and scaling of the skin. Histology of skin lesions shows increased proliferation of the cells in the
30 epidermis, the uppermost layer of skin, together with the abnormal presence of inflammatory cells, including lymphocytes, in the dermis, the layer of skin below the epidermis. While the cause of the disease is unclear, psoriasis is associated with a disturbance of the immune system involving T lymphocytes. The disease occurs more frequently in family members, indicating the involvement of a genetic factor as well. Mice with the *fsn* gene mutation have not only a
35 psoriatic-like skin disease but also other abnormalities involving cells of the immune and

5 hematopoietic system. These mice have markedly increased numbers of lymphocytes associated with enlarged lymphoid organs, including the spleen and lymph nodes. In addition, their livers are enlarged, and the mice are anaemic. Genes and proteins expressed in abnormal lymph nodes of *fsn*^{-/-} mice may thus influence the development or function of cells of the immune and hematopoietic system, the response of these cells in inflammatory disorders, and the responses of
10 skin and other connective tissue cells to inflammatory signals.

There is a need in the art to identify genes encoding proteins that function to modulate all cells of the immune system. These proteins from normal or abnormal lymph nodes may be useful in modifying the immune responses to tumour cells or infectious agents such as bacteria, viruses, protozoa and worms. Such proteins may be useful in the treatment of disorders where
15 the immune system initiates unfavourable reactions to the body, including Type I hypersensitivity reactions (such as hay fever, eczema, allergic rhinitis and asthma), and Type II hypersensitivity reactions (such as transfusion reactions and haemolytic disease of newborns). Other unfavourable reactions are initiated during Type III reactions, which are due to immune complexes forming in infected organs during persistent infection or in the lungs following
20 repeated inhalation of materials from moulds, plants or animals, and in Type IV reactions in diseases such as leprosy, schistosomiasis and dermatitis.

Novel proteins of the immune system may also be useful in treating autoimmune diseases where the body recognises itself as foreign. Examples of such diseases include rheumatoid arthritis, Addison's disease, ulcerative colitis, dermatomyositis and lupus. Such proteins may
25 also be useful during tissue transplantation, where the body will often recognise the transplanted tissue as foreign and attempt to kill it, and also in bone marrow transplantation when there is a high risk of graft-versus-host disease where the transplanted cells attack their host cells, often causing death.

There thus remains a need in the art for the identification and isolation of genes encoding
30 proteins expressed in cells of the immune system for use in the development of therapeutic agents for the treatment of disorders including those associated with the immune system.

5 Summary of the Invention

The present invention provides polypeptides expressed in lymph node stromal cells of *fsn* ^{-/-} mice, together with polynucleotides encoding such polypeptides, expression vectors and host cells comprising such polynucleotides, and methods for their use.

10 In specific embodiments, isolated polypeptides are provided that comprise an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 11-20, 30-38 and 47-53, and variants of such sequences, as defined herein. Isolated polypeptides which comprise at least a functional portion of a polypeptide comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 11-20, 30-38 and 47-53; and (b) variants of a sequence of SEQ ID NO: 11-20, 30-38 and 47-53, as defined herein,
15 are also provided.

In other embodiments, the present invention provides isolated polynucleotides comprising a nucleotide sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46; (b) complements of sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46; (c) reverse complements of sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46; (d) reverse sequences of sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46; and (e) variants of the sequences of (a) – (d), as defined herein.
20

In related embodiments, the present invention provides expression vectors comprising the above polynucleotides, together with host cells transformed with such vectors.

As detailed below, the isolated polynucleotides and polypeptides of the present invention
25 may be usefully employed in the preparation of therapeutic agents for the treatment of immunological disorders.

In related embodiments, methods for modulating the growth of blood vessels, and for the treatment of disorders such as inflammatory disorders, disorders of the immune system, cancer, tumour-necrosis factor-mediated disorders, and viral disorders are provided. Examples of such
30 disorders include HIV-infection; epithelial, lymphoid, myeloid, stromal and neuronal cancers; arthritis; inflammatory bowel disease; and cardiac failure.

The above-mentioned and additional features of the present invention, together with the manner of obtaining them, will be best understood by reference to the following more detailed description. All references disclosed herein are hereby incorporated by reference in their entirety
35 as if each was incorporated individually.

Detailed Description of the Invention

In one aspect, the present invention provides polynucleotides isolated from lymph node stromal cells of *fsn* ^{-/-} mice and isolated polypeptides encoded by such polynucleotides.

The term "polynucleotide(s)," as used herein, means a single or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and corresponding RNA molecules, including HnRNA and mRNA molecules, both sense and anti-sense strands, and comprehends cDNA, genomic DNA and recombinant DNA, as well as wholly or partially synthesized polynucleotides. An HnRNA molecule contains introns and corresponds to a DNA molecule in a generally one-to-one manner. An mRNA molecule corresponds to an HnRNA and DNA molecule from which the introns have been excised. A polynucleotide may consist of an entire gene, or any portion thereof. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all such operable anti-sense fragments. Anti-sense polynucleotides and techniques involving anti-sense polynucleotides are well known in the art and are described, for example, in Robinson-Benion *et al.*, *Methods in Enzymol.* 254: 363-375, 1995 and Kawasaki *et al.*, *Artific. Organs* 20: 836-848, 1996.

In specific embodiments, the isolated polynucleotides of the present invention comprise a DNA sequence selected from the group consisting of sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46.

Complements of such isolated polynucleotides, reverse complements of such isolated polynucleotides and reverse sequences of such isolated polynucleotides are also provided, together with polynucleotides comprising at least a specified number of contiguous residues (x-mers) of any of the above-mentioned polynucleotides, extended sequences corresponding to any of the above polynucleotides, antisense sequences corresponding to any of the above polynucleotides, and variants of any of the above polynucleotides, as that term is described in this specification.

The definition of the terms "complement", "reverse complement" and "reverse sequence", as used herein, is best illustrated by the following example. For the sequence 5' AGGACC 3', the complement, reverse complement and reverse sequence are as follows:

5

complement	3' TCCTGG 5'
reverse complement	3' GGTCCT 5'
reverse sequence	5' CCAGGA 3'.

Some of the polynucleotides of the present invention are "partial" sequences, in that they do not represent a full length gene encoding a full length polypeptide. Such partial sequences may be extended by analyzing and sequencing various DNA libraries using primers and/or probes and well known hybridization and/or PCR techniques. Partial sequences may be extended until an open reading frame encoding a polypeptide, a full length polynucleotide and/or gene capable of expressing a polypeptide, or another useful portion of the genome is identified. Such extended sequences, including full length polynucleotides and genes, are described as "corresponding to" a sequence identified as one of the sequences of SEQ ID NO: 1-10, 21-29 and 39-46, or a variant thereof, or a portion of one of the sequences of SEQ ID NO: 1-10, 21-29 and 39-46, or a variant thereof, when the extended polynucleotide comprises an identified sequence or its variant, or an identified contiguous portion (x-mer) of one of the sequences of SEQ ID NO: 1-10, 21-29 and 39-46, or a variant thereof. Such extended polynucleotides may have a length of from about 50 to about 4,000 nucleic acids or base pairs, and preferably have a length of less than about 4,000 nucleic acids or base pairs, more preferably yet a length of less than about 3,000 nucleic acids or base pairs, more preferably yet a length of less than about 2,000 nucleic acids or base pairs. Under some circumstances, extended polynucleotides of the present invention may have a length of less than about 1,800 nucleic acids or base pairs, preferably less than about 1,600 nucleic acids or base pairs, more preferably less than about 1,400 nucleic acids or base pairs, more preferably yet less than about 1,200 nucleic acids or base pairs, and most preferably less than about 1,000 nucleic acids or base pairs.

Similarly, RNA sequences, reverse sequences, complementary sequences, antisense sequences, and the like, corresponding to the polynucleotides of the present invention, may be routinely ascertained and obtained using the cDNA sequences identified as SEQ ID NO: 1-10, 21-29 and 39-46.

The polynucleotides identified as SEQ ID NO: 1-10, 21-29 and 39-46 may contain open reading frames ("ORFs") or partial open reading frames encoding polypeptides. Open reading frames may be identified using techniques that are well known in the art. These techniques include, for example, analysis for the location of known start and stop codons, most likely

5 reading frame identification based on codon frequencies, etc. Suitable tools and software for ORF analysis are available, for example, on the Internet at <http://www.ncbi.nlm.nih.gov/gorf/gorf.html>. Open reading frames and portions of open reading frames may be identified in the polynucleotides of the present invention. Once a partial open reading frame is identified, the polynucleotide may be extended in the area of the partial open
10 reading frame using techniques that are well known in the art until the polynucleotide for the full open reading frame is identified. Thus, open reading frames encoding polypeptides may be identified using the polynucleotides of the present invention.

Once open reading frames are identified in the polynucleotides of the present invention, the open reading frames may be isolated and/or synthesized. Expressible genetic constructs
15 comprising the open reading frames and suitable promoters, initiators, terminators, etc., which are well known in the art, may then be constructed. Such genetic constructs may be introduced into a host cell to express the polypeptide encoded by the open reading frame. Suitable host cells may include various prokaryotic and eukaryotic cells, including plant cells, mammalian cells, bacterial cells, algae and the like.

20 In another aspect, the present invention provides isolated polypeptides encoded, or partially encoded, by the above polynucleotides. The term "polypeptide", as used herein, encompasses amino acid chains of any length including full length proteins, wherein amino acid residues are linked by covalent peptide bonds. Polypeptides of the present invention may be naturally purified products, or may be produced partially or wholly using recombinant
25 techniques. The term "polypeptide encoded by a polynucleotide" as used herein, includes polypeptides encoded by a nucleotide sequence which includes the partial isolated DNA sequences of the present invention. In specific embodiments, the inventive polypeptides comprise an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 11-20, 30-38, 47-53 and variants of such sequences.

30 Polypeptides encoded by the polynucleotides of the present invention may be expressed and used in various assays to determine their biological activity. Such polypeptides may be used to raise antibodies, to isolate corresponding interacting proteins or other compounds, and to quantitatively determine levels of interacting proteins or other compounds.

All of the polynucleotides and polypeptides described herein are isolated and purified, as
35 those terms are commonly used in the art. Preferably, the polypeptides and polynucleotides are at

- 5 least about 80% pure, more preferably at least about 90% pure, and most preferably at least about 99% pure.

As used herein, the term "variant" comprehends nucleotide or amino acid sequences different from the specifically identified sequences, wherein one or more nucleotides or amino acid residues is deleted, substituted, or added. Variants may be naturally occurring allelic variants, or non-naturally occurring variants. Variant sequences (polynucleotide or polypeptide) preferably exhibit at least 50%, more preferably at least 75%, and most preferably at least 90% identity to a sequence of the present invention. The percentage identity is determined by aligning the two sequences to be compared, determining the number of identical residues in the aligned portion, dividing that number by the total length of the inventive, or queried, sequence and multiplying the result by 100.

Polynucleotide or polypeptide sequences may be aligned, and percentage of identical residues in a specified region may be determined against another polynucleotide, using computer algorithms that are publicly available. Two exemplary algorithms for aligning and identifying the similarity of polynucleotide sequences are the BLASTN and FASTA algorithms. Polynucleotides may also be analyzed using the BLASTX algorithm, which compares the six-frame conceptual translation products of a nucleotide query sequence (both strands) against a protein sequence database. The similarity of polypeptide sequences may be examined using the BLASTP or FASTX algorithms. Both the BLASTN and BLASTP software are available on the NCBI anonymous FTP server (<ftp://ncbi.nlm.nih.gov>) under /blast/executables/. The BLASTN algorithm version 2.0.6 [Sept-16-1998], set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of variants according to the present invention. The use of the BLAST family of algorithms, including BLASTN and BLASTP, is described at NCBI's website at URL <http://www.ncbi.nlm.nih.gov/BLAST/newblast.html> and in the publication of Altschul *et al.*, "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", *Nucleic Acids Res.* 25:3389-3402, 1997. The computer algorithm FASTA is available on the Internet at the ftp site <ftp://ftp.virginia.edu/pub/fasta/>. Version 3.1t11, August 1998, set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of variants according to the present invention. The use of the FASTA algorithm is described in Pearson and Lipman, "Improved Tools for Biological

- 5 Sequence Analysis,” *Proc. Natl. Acad. Sci. USA* 85:2444-2448, 1988 and Pearson, “Rapid and Sensitive Sequence Comparison with FASTP and FASTA,” *Methods in Enzymol.* 183:63-98, 1990. The use of the FASTX algorithm is described in Pearson *et al.*, “Comparison of DNA sequences with protein sequences,” *Genomics* 46:24-36, 1997.

The following running parameters are preferred for determination of alignments and similarities using BLASTN that contribute to the E values and percentage identity: Unix running
10 command: `blastall -p blastn -d embldb -e 10 -G 0 -E 0 -r 1 -v 30 -b 30 -i queryseq -o results;`
and parameter default values:

- p Program Name [String]
- d Database [String]
- 15 -e Expectation value (E) [Real]
- G Cost to open a gap (zero invokes default behavior) [Integer]
- E Cost to extend a gap (zero invokes default behavior) [Integer]
- r Reward for a nucleotide match (BLAST only) [Integer]
- v Number of one-line descriptions (V) [Integer]
- 20 -b Number of alignments to show (B) [Integer]
- i Query File [File In]
- o BLAST report Output File [File Out] Optional

For BLASTP the following running parameters are preferred: `blastall -p blastp -d swissprot -e 10 -G 0 -E 0 -v 30 -b 30 -i queryseq -o results`

- 25 -p Program Name [String]
- d Database [String]
- e Expectation value (E) [Real]
- G Cost to open a gap (zero invokes default behavior) [Integer]
- E Cost to extend a gap (zero invokes default behavior) [Integer]
- 30 -v Number of one-line descriptions (v) [Integer]
- b Number of alignments to show (b) [Integer]
- I Query File [File In]
- o BLAST report Output File [File Out] Optional

The “hits” to one or more database sequences by a queried sequence produced by
35 BLASTN, BLASTP, FASTA, or a similar algorithm, align and identify similar portions of

5 sequences. The hits are arranged in order of the degree of similarity and the length of sequence overlap. Hits to a database sequence generally represent an overlap over only a fraction of the sequence length of the queried sequence.

The BLASTN and FASTA algorithms also produce "Expect" values for alignments. The Expect value (E) indicates the number of hits one can "expect" to see over a certain number of
10 contiguous sequences by chance when searching a database of a certain size. The Expect value is used as a significance threshold for determining whether the hit to a database, such as the preferred EMBL database, indicates true similarity. For example, an E value of 0.1 assigned to a hit is interpreted as meaning that in a database of the size of the EMBL database, one might expect to see 0.1 matches over the aligned portion of the sequence with a similar score simply by
15 chance. By this criterion, the aligned and matched portions of the sequences then have a probability of 90% of being the same. For sequences having an E value of 0.01 or less over aligned and matched portions, the probability of finding a match by chance in the EMBL database is 1% or less using the BLASTN or FASTA algorithm.

According to one embodiment, "variant" polynucleotides, with reference to each of the
20 polynucleotides of the present invention, preferably comprise sequences having the same number or fewer nucleic acids than each of the polynucleotides of the present invention and producing an E value of 0.01 or less when compared to the polynucleotide of the present invention. That is, a variant polynucleotide is any sequence that has at least a 99% probability of being the same as the polynucleotide of the present invention, measured as having an E value of 0.01 or less using
25 the BLASTN or FASTA algorithms set at the default parameters. According to a preferred embodiment, a variant polynucleotide is a sequence having the same number or fewer nucleic acids than a polynucleotide of the present invention that has at least a 99% probability of being the same as the polynucleotide of the present invention, measured as having an E value of 0.01 or less using the BLASTN or FASTA algorithms set at the default parameters.

30 Alternatively, variant polynucleotide sequences hybridize to the recited polynucleotide sequence under stringent conditions. As used herein, "stringent conditions" refers to prewashing in a solution of 6X SSC, 0.2% SDS; hybridizing at 65°C, 6X SSC, 0.2% SDS overnight; followed by two washes of 30 minutes each in 1X SSC, 0.1% SDS at 65 °C and two washes of 30 minutes each in 0.2X SSC, 0.1% SDS at 65 °C.

5 The present invention also encompasses polynucleotides that differ from the disclosed sequences but that, as a consequence of the degeneracy of the genetic code, encode a polypeptide which is the same as that encoded by a polynucleotide of the present invention. Thus, polynucleotides comprising sequences that differ from the polynucleotide sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46, or complements, reverse sequences, or reverse
10 complements thereof, as a result of conservative substitutions are contemplated by and encompassed within the present invention. Additionally, polynucleotides comprising sequences that differ from the polynucleotide sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46, or complements, reverse complements or reverse sequences thereof, as a result of deletions and/or insertions totaling less than 10% of the total sequence length are also contemplated by and
15 encompassed within the present invention. Similarly, polypeptides comprising sequences that differ from the polypeptide sequences provided in SEQ ID NO: 11-20, 30-38 and 47-53, as a result of amino acid substitutions, insertions, and/or deletions totaling less than 10% of the total sequence length are contemplated by and encompassed within the present invention.

 Polynucleotides of the present invention also comprehend polynucleotides comprising at
20 least a specified number of contiguous residues (*x*-mers) of any of the polynucleotides identified as SEQ ID NO: 1-10, 21-29 and 39-46, complements, reverse sequences, and reverse complements of such sequences, and their variants. Similarly, polypeptides of the present invention comprehend polypeptides comprising at least a specified number of contiguous residues (*x*-mers) of any of the polypeptides identified as SEQ ID NO: 11-20, 30-38 and 47-53,
25 and their variants. As used herein, the term "*x*-mer," with reference to a specific value of "*x*," refers to a sequence comprising at least a specified number ("*x*") of contiguous residues of any of the polynucleotides identified as SEQ ID NO: 1-10, 21-29 and 39-46, or the polypeptides identified as SEQ ID NO: 11-20, 30-38 and 47-53. According to preferred embodiments, the value of *x* is preferably at least 20, more preferably at least 40, more preferably yet at least 60,
30 and most preferably at least 80. Thus, polynucleotides and polypeptides of the present invention comprise a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a 250-mer, a 300-mer, 400-mer, 500-mer or 600-mer of a polynucleotide or polypeptide identified as SEQ ID NO: 1-53, and variants thereof.

 The inventive polynucleotides may be isolated by high throughput sequencing of cDNA
35 libraries prepared from lymph node stromal cells of *fsn* ^{-/-} mice as described below in Example

5 1. Alternatively, oligonucleotide probes based on the sequences provided in SEQ ID NO: 1-10,
21-29 and 39-46 can be synthesized and used to identify positive clones in either cDNA or
genomic DNA libraries from lymph node stromal cells of *fsn* ^{-/-} mice by means of hybridization
or polymerase chain reaction (PCR) techniques. Probes can be shorter than the sequences
provided herein but should be at least about 10, preferably at least about 15 and most preferably
10 at least about 20 nucleotides in length. Hybridization and PCR techniques suitable for use with
such oligonucleotide probes are well known in the art (see, for example, Mullis *et al.*, *Cold
Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press,
NY, 1989; Sambrook *et al.*, *Molecular cloning - a laboratory manual*, Cold Spring Harbor
Laboratory Press, Cold Spring Harbor, NY, 1989). Positive clones may be analyzed by
15 restriction enzyme digestion, DNA sequencing or the like.

The polynucleotides of the present invention may alternatively be synthesized using
techniques that are well known in the art. The polynucleotides may be synthesized, for example,
using automated oligonucleotide synthesizers (*e.g.*, Beckman Oligo 1000M DNA Synthesizer) to
obtain polynucleotide segments of up to 50 or more nucleic acids. A plurality of such
20 polynucleotide segments may then be ligated using standard DNA manipulation techniques that
are well known in the art of molecular biology. One conventional and exemplary polynucleotide
synthesis technique involves synthesis of a single stranded polynucleotide segment having, for
example, 80 nucleic acids, and hybridizing that segment to a synthesized complementary 85
nucleic acid segment to produce a 5 nucleotide overhang. The next segment may then be
25 synthesized in a similar fashion, with a 5 nucleotide overhang on the opposite strand. The
"sticky" ends ensure proper ligation when the two portions are hybridized. In this way, a
complete polynucleotide of the present invention may be synthesized entirely *in vitro*.

Polypeptides of the present invention may be produced recombinantly by inserting a
DNA sequence that encodes the polypeptide into an expression vector and expressing the
30 polypeptide in an appropriate host. Any of a variety of expression vectors known to those of
ordinary skill in the art may be employed. Expression may be achieved in any appropriate host
cell that has been transformed or transfected with an expression vector containing a DNA
molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast
and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, insect, yeast or a
35 mammalian cell line such as COS or CHO. The DNA sequences expressed in this manner may

5 encode naturally occurring polypeptides, portions of naturally occurring polypeptides, or other variants thereof.

In a related aspect, polypeptides are provided that comprise at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 11-20, 30-38 and 47-53 and variants thereof. As used herein, the
 10 "functional portion" of a polypeptide is that portion which contains the active site essential for affecting the function of the polypeptide, for example, the portion of the molecule that is capable of binding one or more reactants. The active site may be made up of separate portions present on one or more polypeptide chains and will generally exhibit high binding affinity. Such functional portions generally comprise at least about 5 amino acid residues, more preferably at least about
 15 10, and most preferably at least about 20 amino acid residues. Functional portions of the inventive polypeptides may be identified by first preparing fragments of the polypeptide, by either chemical or enzymatic digestion of the polypeptide or mutation analysis of the polynucleotide that encodes for the polypeptide, and subsequently expressing the resultant mutant polypeptides. The polypeptide fragments or mutant polypeptides are then tested to
 20 determine which portions retain the biological activity of the full-length polypeptide.

Portions and other variants of the inventive polypeptides may be generated by synthetic or recombinant means. Synthetic polypeptides having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may be generated using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any
 25 of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain (Merrifield, *J. Am. Chem. Soc.* 85:2149-2154, 1963). Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems, Inc. (Foster City, CA), and may be operated according to the manufacturer's
 30 instructions. Variants of a native polypeptide may be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see, for example, Kunkel, *Proc. Natl. Acad. Sci. USA* 82:488-492, 1985). Sections of DNA sequence may also be removed using standard techniques to permit preparation of truncated polypeptides.

Since the polynucleotide sequences of the present invention have been derived from *f/sn* -
 35 /- mouse lymph node stromal cells, they likely encode proteins that have important role(s) in

5 growth and development of the immune system, and in responses of the immune system to tissue injury and inflammation as well as other disease states. Some of the polynucleotides contain sequences that code for signal sequences, or transmembrane domains, which identify the protein products as secreted molecules or receptors. Such protein products are likely to be growth factors, cytokines, or their cognate receptors. The polypeptide sequence of SEQ ID NO: 13 has
10 more than 25% identity to known members of the tumour necrosis factor (TNF) receptor family of proteins, with the polypeptides of SEQ ID NO: 30, 31, 32 and 33 having more than 25% identity to known members of the fibroblast growth factor (FGF) receptor family of proteins, and the polypeptide of SEQ ID NO: 38 having more than 25% identity to known members of the WDNM1 family of proteins. These inventive polypeptides are thus likely to have similar
15 biological functions.

In particular, the inventive polypeptides may have important roles in processes such as: modulation of immune responses; differentiation of precursor immune cells into specialized cell types; cell migration; cell proliferation and cell-cell interaction. The polypeptides may be important in the defence of the body against infectious agents, and thus be of importance in
20 maintaining a disease-free environment. These polypeptides may act as modulators of skin cells, especially since immune cells are known to infiltrate skin during tissue insult, causing growth and differentiation of skin cells. In addition, these proteins may be immunologically active, making them important therapeutic targets in a large range of disease states.

In one aspect, the present invention provides methods for using one or more of the
25 inventive polypeptides or polynucleotides to treat disorders in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human.

In this aspect, the polypeptide or polynucleotide is generally present within a pharmaceutical composition or a vaccine. Pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the above sequences (or variants thereof), and a physiologically acceptable carrier. Vaccines may comprise one or more of the
30 above polypeptides and a non-specific immune response amplifier, such as an adjuvant or a liposome, into which the polypeptide is incorporated.

Alternatively, a vaccine or pharmaceutical composition of the present invention may contain DNA encoding one or more polypeptides as described above, such that the polypeptide is
35 generated *in situ*. In such vaccines and pharmaceutical compositions, the DNA may be present

5 within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, and bacterial and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminator signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus Calmette-Guerin*) that expresses an immunogenic
10 portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other poxvirus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic, or defective, replication competent virus. Techniques for incorporating DNA into such expression systems are well known in the art. The DNA may also be "naked," as described, for example, in Ulmer *et al.*, *Science*
15 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

Routes and frequency of administration, as well as dosage, will vary from individual to individual. In general, the pharmaceutical compositions and vaccines may be administered by
20 injection (*e.g.*, intradermal, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. In general, the amount of polypeptide present in a dose (or produced *in situ* by the DNA in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg per kg of host, and preferably from about 100 pg to about 1 µg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from
25 about 0.1 ml to about 2 ml.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a lipid, a wax or a buffer. For oral
30 administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactic galactide) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and
35 5,075,109.

5 Any of a variety of adjuvants may be employed in the vaccines derived from this invention to non-specifically enhance the immune response. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a non-specific stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *M. tuberculosis*. Suitable adjuvants are commercially available as, for example, Freund's
10 Incomplete Adjuvant and Freund's Complete Adjuvant (Difco Laboratories, Detroit, MI), and Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ). Other suitable adjuvants include alum, biodegradable microspheres, monophosphoryl lipid A and Quil A.

The polynucleotides of the present invention may also be used as markers for tissue, as chromosome markers or tags, in the identification of genetic disorders, and for the design of
15 oligonucleotides for examination of expression patterns using techniques well known in the art, such as the microarray technology available from Synteni (Palo Alto, CA). Partial polynucleotide sequences disclosed herein may be employed to obtain full length genes by, for example, screening of DNA expression libraries, and to isolate homologous DNA sequences from other species using hybridization probes or PCR primers based on the inventive sequences.

20 The isolated polynucleotides of the present invention also have utility in genome mapping, in physical mapping, and in positional cloning of genes. As detailed below, the polynucleotide sequences identified as SEQ ID NO: 1-10, 21-29 and 39-46, and their variants, may be used to design oligonucleotide probes and primers. Oligonucleotide probes designed using the polynucleotides of the present invention may be used to detect the presence and
25 examine the expression patterns of genes in any organism having sufficiently similar DNA and RNA sequences in their cells using techniques that are well known in the art, such as slot blot DNA hybridization techniques. Oligonucleotide primers designed using the polynucleotides of the present invention may be used for PCR amplifications. Oligonucleotide probes and primers designed using the polynucleotides of the present invention may also be used in connection with
30 various microarray technologies, including the microarray technology of Synteni (Palo Alto, California).

As used herein, the term "oligonucleotide" refers to a relatively short segment of a polynucleotide sequence, generally comprising between 6 and 60 nucleotides, and comprehends both probes for use in hybridization assays and primers for use in the amplification of DNA by
35 polymerase chain reaction. An oligonucleotide probe or primer is described as "corresponding

5 to" a polynucleotide of the present invention, including one of the sequences set out as SEQ ID NO: 1-10, 21-29 and 39-46, or a variant thereof, if the oligonucleotide probe or primer, or its complement, is contained within one of the sequences set out as SEQ ID NO: 1-10, 21-29 and 39-46, or a variant of one of the specified sequences. Oligonucleotide probes and primers of the present invention are substantially complementary to a polynucleotide disclosed herein.

10 Two single stranded sequences are said to be substantially complementary when the nucleotides of one strand, optimally aligned and compared, with the appropriate nucleotide insertions and/or deletions, pair with at least 80%, preferably at least 90% to 95% and more preferably at least 98% to 100% of the nucleotides of the other strand. Alternatively, substantial complementarity exists when a first DNA strand will selectively hybridize to a second DNA
15 strand under stringent hybridization conditions. Stringent hybridization conditions for determining complementarity include salt conditions of less than about 1 M, more usually less than about 500 mM, and preferably less than about 200 mM. Hybridization temperatures can be as low as 5°C, but are generally greater than about 22°C, more preferably greater than about 30°C, and most preferably greater than about 37°C. Longer DNA fragments may require higher
20 hybridization temperatures for specific hybridization. Since the stringency of hybridization may be affected by other factors such as probe composition, presence of organic solvents and extent of base mismatching, the combination of parameters is more important than the absolute measure of any one alone.

In specific embodiments, the oligonucleotide probes and/or primers comprise at least
25 about 6 contiguous residues, more preferably at least about 10 contiguous residues, and most preferably at least about 20 contiguous residues complementary to a polynucleotide sequence of the present invention. Probes and primers of the present invention may be from about 8 to 100 base pairs in length or, preferably from about 10 to 50 base pairs in length or, more preferably from about 15 to 40 base pairs in length. The probes can be easily selected using procedures
30 well known in the art, taking into account DNA-DNA hybridization stringencies, annealing and melting temperatures, and potential for formation of loops and other factors, which are well known in the art. Tools and software suitable for designing probes, and especially suitable for designing PCR primers, are available on the Internet, for example, at URL <http://www.horizonpress.com/pct/>. Preferred techniques for designing PCR primers are also

disclosed in Dieffenbach, CW and Dyksler, GS. *PCR Primer: a laboratory manual*, CSHL Press: Cold Spring Harbor, NY, 1995.

A plurality of oligonucleotide probes or primers corresponding to a polynucleotide of the present invention may be provided in a kit form. Such kits generally comprise multiple DNA or oligonucleotide probes, each probe being specific for a polynucleotide sequence. Kits of the present invention may comprise one or more probes or primers corresponding to a polynucleotide of the present invention, including a polynucleotide sequence identified in SEQ ID NO: 1-10, 21-29 and 39-46.

In one embodiment useful for high-throughput assays, the oligonucleotide probe kits of the present invention comprise multiple probes in an array format, wherein each probe is immobilized at a predefined, spatially addressable location on the surface of a solid substrate. Array formats which may be usefully employed in the present invention are disclosed, for example, in U.S. Patents No. 5,412,087 and 5,545,451, and PCT Publication No. WO 95/00450, the disclosures of which are hereby incorporated by reference.

The polynucleotides of the present invention may also be used to tag or identify an organism or reproductive material therefrom. Such tagging may be accomplished, for example, by stably introducing a non-disruptive non-functional heterologous polynucleotide identifier into an organism, the polynucleotide comprising one of the polynucleotides of the present invention.

The polypeptides provided by the present invention may additionally be used in assays to determine biological activity, to raise antibodies, to isolate corresponding ligands or receptors, in assays to quantify levels of protein or cognate corresponding ligand or receptor, as anti-inflammatory agents, and in compositions for the treatment of diseases of skin, connective tissue and the immune system.

Example 1

ISOLATION OF cDNA SEQUENCES FROM LYMPH NODE STROMAL CELL EXPRESSION LIBRARIES

The cDNA sequences of the present invention were obtained by high-throughput sequencing of cDNA expression libraries constructed from rodent *fsn* ^{-/-} lymph node stromal cells as described below.

5 *cDNA Libraries from Lymph Node Stromal Cells (MLSA and MLSE)*

Lymph nodes were removed from flaky skin *fsn* ^{-/-} mice, the cells dissociated and the resulting single cell suspension placed in culture. After four passages, the cells were harvested. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, MD), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, CA),
 10 according to the manufacturer's specifications. A cDNA expression library (referred to as the MLSA library) was then prepared from the mRNA by Reverse Transcriptase synthesis using a Lambda ZAP Express cDNA library synthesis kit (Stratagene, La Jolla, CA). A second cDNA expression library, referred to as the MLSE library, was prepared exactly as above except that the cDNA was inserted into the mammalian expression vector pcDNA3 (Invitrogen, Carlsbad
 15 CA).

The nucleotide sequence of the cDNA clone isolated from the MLSE library is given in SEQ ID NO: 1, with the corresponding amino acid sequence being provided in SEQ ID NO: 11. The nucleotide sequences of the cDNA clones isolated from the MLSA library are given in SEQ ID NO: 2-10, 21-23 and 28, with the corresponding amino acid sequences being provided in
 20 SEQ ID NO: 12-20, 30-32 and 37, respectively.

Subtracted cDNA Library from flaky skin Lymph Node Stromal Cells (MLSS)

Stromal cells from flaky skin mice lymph nodes and 3T3 fibroblasts were grown in culture and the total RNA extracted from these cells using established protocols. Total RNA
 25 from both populations was isolated using TRIzol Reagent (Gibco BRL Life Technologies, Gaithersburg, MD) and used to obtain mRNA using either a Poly (A) Quik mRNA isolation kit (Stratagene, La Jolla, CA) or Quick Prep^(R) Micro mRNA purification kit (Pharmacia, Uppsala, Sweden). Double-stranded cDNA from flaky skin lymph node stromal cell mRNA was prepared by Reverse Transcriptase synthesis using a lambda ZAP cDNA library synthesis kit (Stratagene)
 30 that had been ligated with *Eco*RI adaptors and digested with *Xho*I to produce double-stranded fragments with *Eco*RI and *Xho*I overhanging ends.

Double-stranded cDNA from 3T3 fibroblasts was prepared using the Superscript II reverse transcriptase (Gibco BRL Life Technologies) followed by treatment with DNA polymerase I and RNaseH (Gibco BRL Life Technologies). Double-stranded 3T3 cDNA was
 35 then digested with restriction endonucleases *Alu*I and *Rsa*I (Gibco BRL Life Technologies) to

5 produce blunt-ended fragments. A 20-fold excess of *AluI* /*RsaI*-digested 3T3 cDNA was hybridized with the *EcoRI/XhoI* flaky skin lymph node stromal cell cDNA in the following hybridisation solution: 50% formamide, 5xSSC, 10mM NaH₂PO₄ pH7.5, 1mM EDTA, 0.1% SDS, 200µg yeast tRNA (Boehringer Mannheim) at 37°C for 24 hours. Hybridized flaky skin lymph node stromal cell cDNA and 3T3 cDNA was then phenol/chloroform extracted and
10 ethanol precipitated. The cDNA was size-fractionated over a Sepharose CL-2B gel filtration column as described in the Lambda ZAP cDNA library synthesis protocol (Stratagene). Flaky skin lymph node stromal cell-specific cDNA was preferentially ligated into ZAP Express vector (Stratagene) by virtue of *EcoRI/XhoI* ends. Chimeric cDNA between flaky skin lymph node stromal cell cDNA and 3T3 cDNA would not be cloned due to non-compatible ends, and the
15 subtracted cDNA library was packaged using Gigapack III Gold packaging extract (Stratagene).

The nucleotide sequences of the cDNA clones isolated from the MLSS library are given in SEQ ID NO: 25-27 and 29, with the corresponding amino acid sequences being provided in SEQ ID NO: 34-36 and 38, respectively.

20

Example 2

CHARACTERIZATION OF ISOLATED CDNA SEQUENCES

The isolated cDNA sequences were compared to sequences in the EMBL DNA database using the computer algorithm BLASTN, and the corresponding predicted protein sequences (DNA translated to protein in each of 6 reading frames) were compared to sequences in the
25 SwissProt database using the computer algorithm BLASTP. Specifically, comparisons of DNA sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46 to sequences in the EMBL (Release 60, September 1999) DNA database, and amino acid sequences provided in SEQ ID NO: 11-20, 30-38 and 47-53 to sequences in the SwissProt and TrEMBL (up to October 20, 1999) databases were made as of December 31, 1999. The cDNA sequences of SEQ ID NO: 1-10, 21-24 and 27-
30 28, and their corresponding predicted amino acid sequences (SEQ ID NO: 11-20, 30-33 and 36-37, respectively) were determined to have less than 75% identity (determined as described above) to sequences in the EMBL and SwissProt databases using the computer algorithms BLASTN and BLASTP, respectively.

Isolated cDNA sequences and their corresponding predicted protein sequences, were
35 computer analyzed for the presence of signal sequences identifying secreted molecules. Isolated

5 cDNA sequences that have a signal sequence at a putative start site within the sequence are provided in SEQ ID NO: 4-6, 9-10, 25-26, 39-41 and 43-45. The isolated cDNA sequences were also computer analyzed for the presence of transmembrane domains coding for putative membrane-bound molecules. Isolated cDNA sequences that have one or more transmembrane domain(s) within the sequence are provided in SEQ ID NO: 1-3, 7, 8, 27 and 41-45.

10 Using automated search programs to screen against sequences coding for known molecules reported to be of therapeutic and/or diagnostic use, the isolated cDNA sequences of SEQ ID NO: 3, 21-24 and 29 were determined to encode predicted protein sequences that appear to be members of the tumour necrosis factor (TNF) receptor family of proteins (SEQ ID NO: 13), the fibroblast growth factor (FGF) receptor family (SEQ ID NO: 30-33) and the WDNM1
15 protein family (SEQ ID NO: 38). A family member is here defined to have at least 20% identical amino acid residues in the translated polypeptide to a known protein or member of a protein family.

As noted above, the isolated cDNA sequence of SEQ ID NO: 3 was determined to encode a predicted protein sequence (SEQ ID NO: 13) that appears to be a member of the TNF-receptor
20 family. Proteins of the TNF/NGF-receptor family are involved in the proliferation, differentiation and death of many cell types including B and T lymphocytes. Residues 18-55 of SEQ ID NO: 13 show a high degree of similarity to the Prosite motif for the TNF/NGF receptor family (Banner *et al.*, *Cell* 73:431-445, 1993). This motif contributes to the ligand binding domain of the molecule and is thus essential to its function. (Gruss and Dower, *Blood* 85:3378-
25 3404, 1995). The polypeptide of SEQ ID NO: 13 is therefore likely to influence the growth, differentiation and activation of several cell types, and may be usefully developed as an agent for the treatment of skin wounds, and the treatment and diagnosis of cancers, inflammatory diseases, and growth and developmental defects.

The isolated cDNA sequence of SEQ ID NO: 29 was determined to encode a predicted
30 protein sequence (SEQ ID NO: 38) that appears to be a member of the WDNM1 protein family. The WDNM1 family of proteins has a conserved arrangement of cysteine residues. The family includes several proteinase inhibitors, suggesting that WDNM1 could encode a product with proteinase inhibiting capacity. The WDNM1 gene has been shown to be down-regulated in metastatic rat mammary adenocarcinomas (Dear and Kefford, *Biochem. Biophys. Res. Comm.*
35 176:247-254, 1991).

5 The isolated cDNA sequence of SEQ ID NO: 21 was determined to encode a predicted protein sequence (SEQ ID NO: 30) that appears to be a member of the fibroblast growth factor (FGF) receptor family of proteins, specifically the FGF receptor 3. Fibroblast growth factor receptors belong to a family of four single membrane-spanning tyrosine kinases (FGFR1 to 4). These receptors serve as high-affinity receptors for 17 growth factors (FGF1 to 17). FGF
10 receptors have important roles in multiple biological processes, including mesoderm induction and patterning, cell growth and migration, organ formation and bone growth (Xu, *Cell Tissue Res.* 296:33-43, 1999). Further analysis of the sequence revealed the presence of a putative transmembrane domain and intracellular domain, similar to other FGF receptors.

 The isolated cDNA sequence of SEQ ID NO: 44 was determined to encode a predicted
15 protein sequence (SEQ ID NO: 52) that appears to be a lysyl oxidase-related protein. Lysyl oxidase is a copper-dependent amine oxidase that has an important role in the formation of connective tissue matrices. The molecule is involved in crosslinking of the extracellular matrix proteins, collagen and elastin (Smith-Mungo and Kagan, *Matrix Biol.* 16:387-398, 1998). Expression of lysyl oxidase is upregulated in many fibrotic diseases, and down regulated in
20 diseases involving impaired copper metabolism. Identification of new lysyl oxidase-related proteins indicates the existence of a multigene family. Experimental evidence suggests that lysyl oxidase may have other important biological functions in addition to its role in cross-linking of collagen and elastin (Smith-Mungo and Kagan, *Matrix Biol.* 16:387-398, 1998).

 The isolated cDNA sequence of SEQ ID NO: 45 was determined to encode a predicted
25 protein sequence (SEQ ID NO: 53) that appears to be a CD99-like protein. CD99, also referred to as MIC2, is a cell surface molecule involved in T cell adhesion processes (Gelin *et al.*, *EMBO J.* 8:3252-3259).

Example 3

ISOLATION OF FULL LENGTH cDNA SEQUENCE OF A MURINE FIBROBLAST GROWTH FACTOR RECEPTOR HOMOLOG

 The full-length cDNA sequence of a murine fibroblast growth factor receptor homolog was isolated as follows.

35 The MLSA cell cDNA library (described in Example 1) was screened with an [α 32 P]-

5 dCTP labeled cDNA probe corresponding to nucleotides 1 to 451 of the coding region within SEQ ID NO: 21. Plaque lifts, hybridization and screening were performed using standard molecular biology techniques. The determined polynucleotide sequence of the full-length murine FGFR gene (referred to as muFGFR- β) is provided in SEQ ID NO: 22, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 31.

10 Analysis of the polynucleotide sequence of SEQ ID NO: 22 revealed the presence of a putative transmembrane domain corresponding to nucleotides 1311 to 1370. The polypeptide sequence (SEQ ID NO: 31) has regions similar to the extracellular domain of the fibroblast growth factor receptor family.

A splice variant of SEQ ID NO: 22 was also isolated from the MLSA cDNA library as
15 described in Example 1. The determined polynucleotide sequence of the splice variant (referred to as FGFR- γ) is provided in SEQ ID NO: 23 and the corresponding predicted amino acid sequence is provided in SEQ ID NO: 32. The splice regions are in an equivalent position to splice sites for previously described FGF receptors (Ornitz, *J. Biol. Chem.* 296:15292-15297, 1996; Wilkie, *Current Biology* 5:500-507, 1995; Miki, *Proc. Natl. Acad. Sci. USA* 89:246-250,
20 1992), thus providing further evidence that this molecule is a FGF receptor homolog.

EXAMPLE 4

ISOLATION OF A HUMAN FGF RECEPTOR HOMOLOG

25 The cDNA EST encoding the partial murine FGF receptor (SEQ ID NO: 21) was used to search the EMBL database (Release 58, March 1999) to identify human EST homologs. The identified EST (Accession Number AI245701) was obtained from Research Genetics, Inc (Huntsville AL) as I.M.A.G.E. Consortium clone ID 1870593. Sequence determination of the complete insert of clone 1870593 resulted in the identification of 520 additional nucleotides.
30 The insert of this clone did not represent the full-length gene. The determined nucleotide sequence of the complete insert of clone 1870593 is given in SEQ ID NO: 24 and the corresponding predicted amino acid sequence in SEQ ID NO: 33.

EXAMPLE 5

CHARACTERIZATION OF MURINE FGF RECEPTOR HOMOLOG

5

The murine FGF receptor homolog, muFGFR- β and splice variant FGFR- γ (SEQ ID NO: 22 and 23, respectively) were expressed in mammalian cells and the purified protein used to determine the ligand binding specificity of the molecules.

10 The extracellular domains of muFGFR- β and FGFR- γ (SEQ ID NO: 22 and 23, respectively) were amplified by PCR using primers MS158 and MS159 (SEQ ID NO: 55 and 56, respectively) and cloned into the expression vector pcDNA3 containing the Fc fragment from human IgG1. These recombinant proteins, referred to as FGFR β Fc and FGFR γ Fc, were expressed in HEK293 cells (ATCC No. CRL-1573, American Type Culture Collection, Manassas, VA) and purified using an Affiprep protein A column (Biorad, Hercules CA).

15 Binding of muFGFR- β to FGF-2 (basic fibroblast growth factor) was demonstrated by co-incubating the purified protein and FGF-2 in the presence of protein G Sepharose (Amersham Pharmacia, Uppsala, Sweden) and resolving complexes formed on denaturing polyacrylamide gels. FGF-2 (2 μ g) was incubated with 5 μ g FGFR β Fc, FGF Receptor 2 (FGFR2Fc) or unrelated protein (MLSA8790Fc) in 5 μ l protein G fast flow beads (Pharmacia, Uppsala, Sweden), PBS and 0.1% Triton X-100 for 60 min at 4°C. The beads were washed three times in 20 μ l loading buffer (0.1 M DTT, 10% sucrose, 60 mM Tris.HCl pH 6.8, 5% SDS and 0.01% bromophenol blue). The samples were analysed on a 12% polyacrylamide gel. FGF-2, FGFR2Fc, FGFR β Fc and MLSA8790Fc (1 μ g of each) were loaded on the gel for comparison. After staining of the gel with Coomassie blue, a doublet of 25 bands were visible in the lane containing FGFR β Fc, indicating that a complex formed between the FGF-2 and the murine FGF receptor homolog FGFR β Fc, and that FGF-2 is a ligand for the novel FGF receptor homolog. A doublet was also observed in the lane containing the FGFR2Fc, which was the positive control. No doublet was observed in the negative control lane containing the MLSA8790Fc protein.

30 The binding specificity of the murine FGF receptor homolog FGFR β Fc was further examined by repeating the experiment described above, replacing the FGF-2 with another known growth factor, epidermal growth factor (EGF). In this experiment, EGF did not bind to FGFR2Fc, the FGFR β Fc or MLSA8790Fc, indicating that binding of FGF-2 to the murine FGF receptor homolog FGFR β Fc was specific.

5

EXAMPLE 6

SEQUENCE DETERMINATION OF A POLYNUCLEOTIDE FRAGMENT
CONTAINING GENOMIC MURINE FGFR β

10

Mouse genomic DNA was isolated from L929 cells using standard techniques. A genomic polynucleotide fragment containing murine FGFR β was PCR amplified using primers MS157 and MS166 (SEQ ID NO: 56 and 57, respectively). The 1.4 kb polynucleotide fragment was cloned into a T-tailed pBluescript SK²⁺ vector. The sequence of the insert of this plasmid was determined using standard primer walking sequencing techniques. The determined base sequence of the genomic fragment containing murine FGFR β is given in SEQ ID NO: 46.

15

CLAIMS:

1. An isolated polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 11-20, 30-38 and 47-53.
2. An isolated polypeptide comprising a sequence selected from the group consisting of:
 - (a) sequences having at least 40% identity to a sequence provided in SEQ ID NO: 11-20, 30-38 and 47-49, 51 and 52 as determined using the computer algorithm BLASTP;
 - (b) sequences having at least 60% identity to a sequence provided in SEQ ID NO: 11-20, 30-38 and 47-53 as determined using the computer algorithm BLASTP;
 - (c) sequences having at least 75% identity to a sequence provided in SEQ ID NO: 11-20, 30-38 and 47-53 as determined using the computer algorithm BLASTP; and
 - (d) sequences having at least 90% identity to a sequence provided in SEQ ID NO: 11-20, 30-38 and 47-53 as determined using the computer algorithm BLASTP.
3. An isolated polynucleotide that encodes a polypeptide according to any one of claims 1 and 2.
4. An isolated polynucleotide of claim 3, wherein the polynucleotide comprises a sequence selected from the group consisting of sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46.
5. An isolated polynucleotide comprising a sequence selected from the group consisting of:
 - (a) complements of a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46;
 - (b) reverse complements of a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46;
 - (c) reverse sequences of a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46;
 - (d) sequences having at least 40% identity to a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46 as determined using the computer algorithm BLASTN;
 - (e) sequences having at least 60% identity to a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46 as determined using the computer algorithm BLASTN;
 - (f) sequences having at least 75% identity to a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46 as determined using the computer algorithm BLASTN; and
 - (g) sequences having at least 90% identity to a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46 as determined using the computer algorithm BLASTN.

6. An isolated polynucleotide comprising a sequence selected from the group consisting of:
(a) sequences that are a 200-mer of an isolated polynucleotide according to any one of claims 3, 4 and 5; (b) sequences that are a 100-mer of an isolated polynucleotide according to any one of claims 3, 4 and 5; and (c) sequences that are a 40-mer of an isolated polynucleotide according to any one of claims 3, 4 and 5.
7. An expression vector comprising an isolated polynucleotide according to any one of claims 3-6.
8. A host cell transformed with an expression vector according to claim 7.
9. An isolated polypeptide comprising at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 11-20, 30-38 and 47-53.
10. A pharmaceutical composition comprising an isolated polypeptide according to any one of claims 1, 2 and 9.
11. A pharmaceutical composition comprising an isolated polynucleotide according to any one of claims 3-6.
12. A method for the treatment of an inflammatory disorder in a patient, comprising administering to the patient a pharmaceutical composition according to any one of claims 10 and 11.
13. A method for modulating the growth of blood vessels in a patient, comprising administering to the patient a pharmaceutical composition according to any one of claims 10 and 11.
14. A method for the treatment of a disorder of the immune system in patient, comprising administering to the patient a pharmaceutical composition according to any one of claims 10 and 11.
15. A method for the treatment of cancer in a patient, comprising administering to the patient a pharmaceutical composition according to any one of claims 10 and 11, wherein the cancer is selected from the group consisting of epithelial, lymphoid, myeloid, stromal and neuronal cancers.
16. A method for the treatment of a tumour necrosis factor-mediated disorder in a patient, comprising administering to the patient a composition comprising an isolated

polypeptide, the polypeptide comprising an amino acid sequence selected from the group consisting of:

- (a) a sequence of SEQ ID NO: 13;
 - (d) sequences having at least 40% identity to the sequence of SEQ ID NO: 13 as determined using the computer algorithm BLASTP;
 - (e) sequences having at least 60% identity to the sequence of SEQ ID NO: 13 as determined using the computer algorithm BLASTP;
 - (f) sequences having at least 75% identity to the sequence of SEQ ID NO: 13 as determined using the computer algorithm BLASTP; and
 - (d) sequences having at least 90% identity to the sequence of SEQ ID NO: 13 as determined using the computer algorithm BLASTP.
17. The method of claim 16, wherein the tumour necrosis factor-mediated disorder is selected from the group consisting of arthritis, inflammatory bowel disease and cardiac failure.
18. A method for the treatment of a viral disorder in a patient, comprising administering to the patient a pharmaceutical composition according to any one of claims 10 and 11.
19. The method of claim 18, wherein the viral disorder is HIV-infection.
20. A method for the treatment of a fibroblast growth factor-mediated disorder in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence selected from the group consisting of:
- (a) a sequence provided in SEQ ID NO: 30-33;
 - (b) sequences having at least 40% identity to a sequence provided in SEQ ID NO: 30-33 as determined using the computer algorithm BLASTP;
 - (c) sequences having at least 60% identity to a sequence provided in SEQ ID NO: 30-33 as determined using the computer algorithm BLASTP;
 - (d) sequences having at least 75% identity to a sequence provided in SEQ ID NO: 30-33 as determined using the computer algorithm BLASTP; and
 - (e) sequences having at least 90% identity to a sequence provided in SEQ ID NO: 30-33 as determined using the computer algorithm BLASTP.

COMPOSITIONS ISOLATED FROM STROMAL CELLS
AND METHODS FOR THEIR USE

Abstract of the Disclosure

Isolated polynucleotides encoding polypeptides expressed in mammalian *fsn* ^{-/-} lymph node stromal cells are provided, together with expression vectors and host cells comprising such isolated polynucleotides. Methods for the use of such polynucleotides and polypeptides are also provided.

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 420
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 1320
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<210> 7
 <211> 1131
 <212> DNA
 <213> Mouse

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 180
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 420
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 1020
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<210> 8
 <211> 1357
 <212> DNA
 <213> Mouse

<400> 8

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720
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1260
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1357

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<210> 9

<211> 815

<212> DNA

<213> Mouse

<400> 9

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120
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240
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300
cagtgaatat cagagcaccg cgaagccttc cgtactgcca aaaactacca cacttatcac

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360
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 480
 atccatgaca accccagccc acagtagttt attgacaact gtaacggttt cagcaactac
 540
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<210> 10
 <211> 1129
 <212> DNA
 <213> Mouse

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 240
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 300
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 360
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 420
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 480
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 780
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<210> 11
 <211> 196
 <212> PRT

<213> Mouse

<400> 11

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Gln	Val	Leu	Ser	Leu	Arg	Asp	Val	Gly	Leu	Gly	Ser	Gly	Ala	Ala	Glu
			20					25					30		
Met	Asp	Phe	Ser	Ala	Phe	Gly	Asn	Leu	Arg	Ala	Leu	Asp	Leu	Ser	Gly
		35					40					45			
Asn	Ser	Leu	Thr	Ser	Phe	Gln	Lys	Phe	Lys	Gly	Ser	Leu	Ala	Leu	Arg
	50					55					60				
Thr	Leu	Asp	Leu	Arg	Arg	Asn	Ser	Leu	Thr	Ala	Leu	Pro	Gln	Arg	Val
65					70					75				80	
Val	Ser	Glu	Gln	Pro	Leu	Arg	Gly	Leu	Gln	Thr	Ile	Tyr	Leu	Ser	Gln
				85					90					95	
Asn	Pro	Tyr	Asp	Cys	Cys	Gly	Val	Glu	Gly	Trp	Gly	Ala	Leu	Gln	Gln
			100					105					110		
His	Phe	Lys	Thr	Val	Ala	Asp	Leu	Ser	Met	Val	Thr	Cys	Asn	Leu	Ser
		115					120					125			
Ser	Lys	Ile	Val	Arg	Val	Val	Glu	Leu	Pro	Glu	Gly	Leu	Pro	Gln	Gly
	130					135					140				
Cys	Lys	Trp	Glu	Gln	Val	Asp	Thr	Gly	Leu	Phe	Tyr	Leu	Val	Leu	Ile
145					150					155					160
Leu	Pro	Ser	Cys	Leu	Thr	Leu	Leu	Val	Ala	Cys	Thr	Val	Val	Phe	Leu
				165					170					175	
Thr	Phe	Lys	Lys	Pro	Leu	Leu	Gln	Val	Ile	Lys	Ser	Arg	Cys	His	Trp
			180					185					190		
Ser	Ser	Ile	Tyr												
			195												

<210> 12

<211> 174

<212> PRT

<213> Mouse

<400> 12

Met	Ala	Pro	Ala	Asn	Leu	Gly	Leu	Thr	Pro	His	Trp	Val	Met	Leu	Leu
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Gly	Ala	Val	Leu	Leu	Leu	Leu	Leu	Ser	Gly	Ala	Ser	Ala	Gln	Glu	Pro
			20					25					30		
Pro	Arg	Val	Gly	Cys	Ser	Glu	Tyr	Thr	Asn	Arg	Ser	Cys	Glu	Glu	Cys
		35					40					45			
Leu	Arg	Asn	Val	Ser	Cys	Leu	Trp	Cys	Asn	Glu	Asn	Lys	Ala	Cys	Met
	50					55					60				
Asp	Tyr	Pro	Val	Arg	Lys	Ile	Leu	Pro	Pro	Ala	Ser	Leu	Cys	Lys	Leu
65					70					75				80	
Ser	Ser	Ala	Arg	Trp	Gly	Val	Cys	Trp	Val	Asn	Phe	Glu	Ala	Leu	Ile
			85						90					95	
Ile	Thr	Met	Ser	Val	Leu	Gly	Gly	Ser	Val	Leu	Leu	Gly	Ile	Thr	Val
			100					105					110		
Cys	Cys	Cys	Tyr	Cys	Cys	Arg	Arg	Lys	Lys	Ser	Arg	Lys	Pro	Asp	Lys
		115					120					125			
Ser	Asp	Glu	Arg	Ala	Met	Arg	Glu	Gln	Glu	Glu	Arg	Arg	Val	Arg	Gln
	130					135					140				
Glu	Glu	Arg	Arg	Ala	Glu	Met	Lys	Ser	Arg	His	Asp	Glu	Ile	Arg	Lys
145					150					155					160
Lys	Tyr	Gly	Leu	Phe	Lys	Glu	Gln	Asn	Pro	Tyr	Glu	Lys	Phe		
				165					170						

<210> 13

<211> 106

<212> PRT

<213> Mouse

<400> 13

Ala	Pro	Gly	Lys	Pro	Cys	Arg	Gly	Leu	Ser	His	Arg	Thr	Cys	Ile	Leu
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

1	5	10	15
Arg Cys Arg	Pro Met Pro Leu Phe	Thr His Pro Ser Pro	Cys His Leu
	20	25	30
Cys Gly Pro	Cys Ser Thr Thr Ser	Pro Ser Thr Trp Val	Leu Cys Pro
	35	40	45
Leu Pro Met	Ser Pro Leu Cys Pro	Thr Cys Val Ser Thr	Met Thr Leu
	50	55	60
Ala Thr Cys	Thr Cys Pro Trp Ser	Thr Thr Cys Pro	Cys Thr Leu Ala
65	70	75	80
Pro Asn His	Gly Ile Ala Ser Asp	Thr Gln Ser Pro	Val Ser Arg Ala
	85	90	95
Glu Ser Val	Gly Gly Pro Ser Leu	Ile Phe	
	100	105	

<210> 14
 <211> 268
 <212> PRT
 <213> Mouse

<400> 14													
Met Ala Leu	Gly Phe Ser	Gln Arg Ser	Arg Met Val	Ala Ala Gly	Ala								
1	5	10	15										
Gly Val Thr	Arg Leu Leu	Val Leu Leu	Leu Met Val	Ala Ala Ala	Pro								
	20	25	30										
Ser Arg Ala	Arg Gly Ser	Gly Cys Arg	Val Gly Ala	Ser Ala Arg	Gly								
	35	40	45										
Thr Gly Ala	Asp Gly Arg	Glu Ala Glu	Gly Cys Gly	Thr Val Ala	Leu								
	50	55	60										
Leu Leu Glu	His Ser Phe	Glu Leu Gly	Asp Gly Ala	Asn Phe Gln	Lys								
65	70	75	80										
Arg Gly Leu	Leu Leu Trp	Asn Gln Gln	Asp Gly Thr	Leu Ser Ala	Thr								
	85	90	95										
Gln Arg Gln	Leu Ser Glu	Glu Glu Arg	Gly Arg Leu	Arg Asp Val	Ala								
	100	105	110										
Ala Val Asn	Gly Leu Tyr	Arg Val Arg	Val Pro Arg	Arg Pro Gly	Thr								
	115	120	125										
Leu Asp Gly	Ser Glu Ala	Gly Gly His	Val Ser Ser	Phe Val Pro	Ala								
	130	135	140										
Cys Ser Leu	Val Glu Ser	His Leu Ser	Asp Gln Leu	Thr Leu His	Val								
145	150	155	160										
Asp Val Ala	Gly Asn Val	Val Gly Leu	Ser Val Val	Val Tyr Pro	Gly								
	165	170	175										
Gly Cys Arg	Gly Ser Glu	Val Glu Asp	Glu Asp Leu	Glu Leu Phe	Asn								
	180	185	190										
Thr Ser Val	Gln Leu Arg	Pro Pro Ser	Thr Ala Pro	Gly Pro Glu	Thr								
	195	200	205										
Ala Ala Phe	Ile Glu Arg	Leu Glu Met	Glu Gln Ala	Gln Lys Ala	Lys								
	210	215	220										
Asn Pro Gln	Glu Gln Lys	Ser Phe Phe	Ala Lys Tyr	Trp Met Tyr	Ile								
225	230	235	240										
Ile Pro Val	Val Leu Phe	Leu Met Met	Ser Gly Ala	Pro Asp Ala	Gly								
	245	250	255										
Gly Gln Gly	Gly Gly Gly	Gly Gly Gly	Gly Ser Ser	Arg									
	260	265											

<210> 15
 <211> 66
 <212> PRT
 <213> Mouse

<400> 15													
Met Asp Phe	Leu Val Leu	Phe Leu Phe	Tyr Leu Ala	Phe Leu Leu	Ile								
1	5	10	15										
Cys Val Val	Leu Ile Cys	Ile Phe Thr	Lys Ser Gln	Arg Leu Lys	Ala								
	20	25	30										
Val Val Leu	Gly Gly Ala	Gln Val Ala	Leu Val Leu	Gly Tyr Cys	Pro								

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 Asp Val Asn Thr Val Leu Gly Ala Ser Leu Glu Gly Ser Gln Asp Lys
 50 55 60
 Gly Met
 65

<210> 16
 <211> 338
 <212> PRT
 <213> Mouse

<400> 16
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 1 5 10 15
 Ala Leu Ile Leu Trp Leu Leu Arg Gly Asp Ser Gly Ala Pro Gly Lys
 20 25 30
 Asp Gly Val Ala Glu Pro Pro Gln Lys Gly Ala Pro Pro Gly Glu Ala
 35 40 45
 Ala Ala Pro Gly Asp Gly Pro Gly Gly Gly Gly Ser Gly Gly Leu Ser
 50 55 60
 Pro Glu Pro Ser Asp Arg Glu Leu Val Ser Lys Ala Glu His Leu Arg
 65 70 75 80
 Glu Ser Asn Gly His Leu Ile Ser Glu Ser Lys Asp Leu Gly Asn Leu
 85 90 95
 Pro Glu Ala Gln Arg Leu Gln Asn Val Gly Ala Asp Trp Val Asn Ala
 100 105 110
 Arg Glu Phe Val Pro Val Gly Lys Ile Pro Asp Thr His Ser Arg Ala
 115 120 125
 Asp Ser Glu Ala Ala Arg Asn Gln Ser Pro Gly Ser His Gly Gly Glu
 130 135 140
 Trp Arg Leu Pro Lys Gly Gln Glu Thr Ala Val Lys Val Ala Gly Ser
 145 150 155 160
 Val Ala Ala Lys Leu Ala Ser Ser Ser Leu Leu Val Asp Arg Ala Lys
 165 170 175
 Ala Val Ser Gln Asp Gln Ala Gly His Glu Asp Trp Glu Val Val Ser
 180 185 190
 Arg His Ser Ser Trp Gly Ser Val Gly Leu Gly Gly Ser Leu Glu Ala
 195 200 205
 Ser Arg Leu Ser Leu Asn Gln Arg Met Asp Asp Ser Thr Asn Ser Leu
 210 215 220
 Val Gly Gly Arg Gly Trp Glu Val Asp Gly Lys Val Ala Ser Leu Lys
 225 230 235 240
 Pro Gln Gln Val Ser Ile Gln Phe Gln Val His Tyr Thr Thr Asn Thr
 245 250 255
 Asp Val Gln Phe Ile Ala Val Thr Gly Asp His Glu Ser Leu Gly Arg
 260 265 270
 Trp Asn Thr Tyr Ile Pro Leu His Tyr Cys Lys Asp Gly Leu Trp Ser
 275 280 285
 His Ser Val Phe Leu Pro Ala Asp Thr Val Val Glu Trp Lys Phe Val
 290 295 300
 Leu Val Glu Asn Lys Glu Val Thr Arg Trp Glu Glu Cys Ser Asn Arg
 305 310 315 320
 Phe Leu Gln Thr Gly His Glu Asp Lys Val Val His Gly Trp Trp Gly
 325 330 335
 Ile His

<210> 17
 <211> 119
 <212> PRT
 <213> Mouse

<400> 17
 Gly Thr Ser Pro Ala Ser Val Leu Arg Ser Val Ser Ser Asp Pro Ser
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 Leu Pro Pro Pro Ser Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu

20 25 30
 Ala Ala Cys Gly Ile Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile
 35 40 45
 Met Leu Gly Ile Phe Phe Asn Val His Ser Ala Val Leu Ile Glu Asp
 50 55 60
 Val Pro Phe Thr Glu Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr
 65 70 75 80
 Asn Leu Tyr Glu Gln Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu
 85 90 95
 Tyr Leu Leu Leu Gly Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys
 100 105 110
 Arg Lys Glu Tyr Met Val Arg
 115

<210> 18
 <211> 280
 <212> PRT
 <213> Mouse

<400> 18
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 Pro Gly Val Ala Tyr Ser Val Ser Leu Pro Ala Ser Phe Leu Glu Asp
 20 25 30
 Val Ala Gly Ser Gly Glu Ala Glu Gly Ser Ser Ala Ser Ser Pro Ser
 35 40 45
 Leu Pro Pro Pro Gly Thr Pro Ala Phe Ser Pro Thr Pro Glu Arg Pro
 50 55 60
 Gln Pro Thr Ala Leu Asp Gly Pro Val Pro Pro Thr Asn Leu Leu Glu
 65 70 75 80
 Gly Ile Met Asp Phe Phe Arg Gln Tyr Val Met Leu Ile Ala Val Val
 85 90 95
 Gly Ser Leu Thr Phe Leu Ile Met Phe Ile Val Cys Ala Ala Leu Ile
 100 105 110
 Thr Arg Gln Lys His Lys Ala Thr Ala Tyr Tyr Pro Ser Ser Phe Pro
 115 120 125
 Glu Lys Lys Tyr Val Asp Gln Arg Asp Arg Ala Gly Gly Pro Arg Thr
 130 135 140
 Phe Ser Glu Val Pro Asp Arg Ala Pro Asp Ser Arg His Glu Glu Gly
 145 150 155 160
 Leu Asp Thr Ser His Gln Leu Gln Ala Asp Ile Leu Ala Ala Thr Gln
 165 170 175
 Asn Leu Arg Ser Pro Ala Arg Ala Leu Pro Gly Asn Gly Glu Gly Ala
 180 185 190
 Lys Pro Val Lys Gly Gly Ser Glu Glu Glu Glu Glu Val Leu Ser
 195 200 205
 Gly Gln Glu Glu Ala Gln Glu Ala Pro Val Cys Gly Val Thr Glu Glu
 210 215 220
 Lys Leu Gly Val Pro Glu Glu Ser Val Ser Ala Glu Ala Glu Gly Val
 225 230 235 240
 Pro Ala Thr Ser Glu Gly Gln Gly Glu Ala Glu Gly Ser Phe Ser Leu
 245 250 255
 Ala Gln Glu Ser Gln Gly Ala Thr Gly Pro Pro Glu Ser Pro Cys Ala
 260 265 270
 Cys Asn Arg Val Ser Pro Ser Val
 275 280

<210> 19
 <211> 188
 <212> PRT
 <213> Mouse

<400> 19
 Met Ala Leu Cys Ala Arg Ala Ala Leu Leu Leu Gly Val Leu Gln Val
 1 5 10 15
 Leu Ala Leu Leu Gly Ala Ala Gln Asp Pro Thr Asp Ala Gln Gly Ser

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<210> 20
<211> 317
<212> PRT
<213> Mouse
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	<400> 20														
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Thr	Val	Gly	Ser 20	Val	Gly	Ala	Val	Met 25	Gly	Ser	Glu	Asp	Ser 30	Val	Pro
Gly	Gly	Val 35	Cys	Trp	Leu	Gln	Gln 40	Gly	Arg	Glu	Ala	Thr 45	Cys	Ser	Leu
Val	Leu 50	Lys	Thr	Arg	Val	Ser 55	Arg	Glu	Glu	Cys	Cys 60	Ala	Ser	Gly	Asn
Ile 65	Asn	Thr	Ala	Trp	Ser 70	Asn	Phe	Thr	His 75	Pro	Gly	Asn	Lys	Ile	Ser 80
Leu	Leu	Gly	Phe 85	Leu	Gly	Leu	Val	His 90	Cys	Leu	Pro	Cys	Lys	Asp 95	Ser
Cys	Asp	Gly	Val 100	Glu	Cys	Gly	Pro	Gly 105	Lys	Ala	Cys	Arg	Asn	Ala	Gly
Gly	Ala	Ser 115	Asn	Asn	Cys	Glu	Cys 120	Val	Pro	Asn	Cys	Glu	Gly 110	Phe	Pro
Ala	Gly 130	Phe	Gln	Val	Cys	Gly 135	Ser	Asp	Gly	Ala	Thr 140	Tyr	Arg	Asp	Glu
Cys 145	Glu	Leu	Arg	Thr 150	Ala	Arg	Cys	Arg	Gly	His 155	Pro	Asp	Leu	Arg	Val 160
Met	Tyr	Arg	Gly 165	Arg	Cys	Gln	Lys	Ser 170	Cys	Ala	Gln	Val	Val	Cys 175	Pro
Arg	Pro	Gln	Ser 180	Cys	Leu	Val	Asp	Gln 185	Thr	Gly	Ser	Ala	His 190	Cys	Val
Val	Cys	Arg 195	Ala	Ala	Pro	Cys	Pro 200	Val	Pro	Ser	Asn	Pro 205	Gly	Gln	Glu
Leu	Cys 210	Gly	Asn	Asn	Asn	Val 215	Thr	Tyr	Ile	Ser	Ser 220	Cys	His	Leu	Arg
Gln 225	Ala	Thr	Cys	Phe	Leu 230	Gly	Arg	Ser	Ile	Gly	Val	Arg	His	Pro	Gly 240
Ile	Cys	Thr	Gly 245	Pro	Lys	Phe	Leu	Lys 250	Ser	Gly	Asp	Ala	Ala 255	Ile	
Val	Asp	Met 260	Val	Pro	Gly	Lys	Pro	Met 265	Cys	Val	Glu	Ser	Phe 270	Ser	Asp
Tyr	Pro	Pro 275	Leu	Gly	Arg	Phe	Ala	Val 280	Arg	Asp	Met	Arg	Gln 285	Thr	Val
Ala	Val 290	Gly	Val	Ile	Lys	Ala 295	Val	Asp	Lys	Lys	Ala	Ala	Gly	Ala	Gly

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<210> 21
 <211> 384
 <212> DNA
 <213> Mouse

<220>
 <221> unsure
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 120
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 240
 ctgcctaggt gcaaatacca tgggctacag ttccgtagc gccttctca ctgtattacc
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<210> 22
 <211> 1967
 <212> DNA
 <213> Mouse

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 720
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 1560
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 1620
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 1680
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 1740
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 1800
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 1860
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 1967

<210> 23
 <211> 1742
 <212> DNA
 <213> Mouse

<400> 23
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 420
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 600
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 660
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 720
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780
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 840
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 960
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 1020
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 1200
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 1260
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 1620
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 1740
 ag
 1742

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 <212> DNA
 <213> Human

<400> 24
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 360
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 420
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 480
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 540
 aagtgcgtgg ccagcgggca ccctcggccc gacatcacgt ggatgaagga cgaccaggcc
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 660
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 720

aacgccacct acaaggtgga tgtgatccag cggacccggt ccaagcccgt gctcacaggc
 780
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 840
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 960
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 1004

<210> 25
 <211> 478
 <212> DNA
 <213> Mouse

<400> 25
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 300
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 360
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 478

<210> 26
 <211> 545
 <212> DNA
 <213> Mouse

<400> 26
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 120
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 180
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 240
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 300
 cctttgtgag gttggaattt aagctccagc agaccaactg cccaagaag gactggaaaa
 360
 agccggagtg cacaatcaaa ccaaaccgga gaaggcgga atgcctggcc tgcattaaaa
 420
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 545

<210> 27
 <211> 2213
 <212> DNA
 <213> Mouse

<400> 27

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 360
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 420
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 480
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1980
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 2100
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<210> 28
 <211> 412
 <212> DNA
 <213> Mouse

<400> 28
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 aagagtctca acaaggcgtc agtggaaaac ctctgactg agattgagat cctcaagggc
 300
 attcggcacc cccatatcgt gcagctgaaa gacttcagat gggacaatga caatatctac
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<210> 29
 <211> 437
 <212> DNA
 <213> Mouse

<400> 29
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 aatttgtgtt gatcaatgct caggagatgg atcctgccct ggcaacatga agtgctgtag
 180
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 240
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 300
 tcacagagcc tgtgcttggc tacttcctag ccctagaatt gcattcttgg acaaggaaga
 360
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 420
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 437

<210> 30
 <211> 126
 <212> PRT
 <213> Mouse

<220>
 <221> UNSURE
 <222> (123)...(123)

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 Gly Arg His Asn Ser Thr Ile Asp Val Gly Gly Gln Lys Phe Val Val
 35 40 45
 Leu Pro Thr Gly Asp Val Trp Ser Arg Pro Asp Gly Ser Tyr Leu Asn
 50 55 60
 Lys Leu Leu Ile Ser Arg Ala Arg Gln Asp Asp Ala Gly Met Tyr Ile
 65 70 75 80
 Cys Leu Gly Ala Asn Thr Met Gly Tyr Ser Phe Arg Ser Ala Phe Leu
 85 90 95
 Thr Val Leu Pro Asp Pro Lys Pro Pro Gly Pro Pro Met Ala Ser Ser
 100 105 110
 Ser Ser Ser Thr Ser Leu Pro Trp Pro Val Xaa Gly Ile Pro
 115 120 125

<210> 31
 <211> 529
 <212> PRT
 <213> Mouse

<400> 31
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 Pro Arg Gln Val Ala Arg Leu Gly Arg Thr Val Arg Leu Gln Cys Pro
 35 40 45
 Val Glu Gly Asp Pro Pro Pro Leu Thr Met Trp Thr Lys Asp Gly Arg
 50 55 60
 Thr Ile His Ser Gly Trp Ser Arg Phe Arg Val Leu Pro Gln Gly Leu
 65 70 75 80
 Lys Val Lys Glu Val Glu Ala Glu Asp Ala Gly Val Tyr Val Cys Lys
 85 90 95
 Ala Thr Asn Gly Phe Gly Ser Leu Ser Val Asn Tyr Thr Leu Ile Ile
 100 105 110
 Met Asp Asp Ile Ser Pro Gly Lys Glu Ser Pro Gly Pro Gly Gly Ser
 115 120 125
 Ser Gly Gly Gln Glu Asp Pro Ala Ser Gln Gln Trp Ala Arg Pro Arg
 130 135 140
 Phe Thr Gln Pro Ser Lys Met Arg Arg Arg Val Ile Ala Arg Pro Val
 145 150 155 160
 Gly Ser Ser Val Arg Leu Lys Cys Val Ala Ser Gly His Pro Arg Pro
 165 170 175
 Asp Ile Met Trp Met Lys Asp Asp Gln Thr Leu Thr His Leu Glu Ala
 180 185 190
 Ser Glu His Arg Lys Lys Lys Trp Thr Leu Ser Leu Lys Asn Leu Lys
 195 200 205
 Pro Glu Asp Ser Gly Lys Tyr Thr Cys Arg Val Ser Asn Lys Ala Gly
 210 215 220
 Ala Ile Asn Ala Thr Tyr Lys Val Asp Val Ile Gln Arg Thr Arg Ser
 225 230 235 240
 Lys Pro Val Leu Thr Gly Thr His Pro Val Asn Thr Thr Val Asp Phe
 245 250 255
 Gly Gly Thr Thr Ser Phe Gln Cys Lys Val Arg Ser Asp Val Lys Pro
 260 265 270
 Val Ile Gln Trp Leu Lys Arg Val Glu Tyr Gly Ser Glu Gly Arg His
 275 280 285
 Asn Ser Thr Ile Asp Val Gly Gly Gln Lys Phe Val Val Leu Pro Thr
 290 295 300
 Gly Asp Val Trp Ser Arg Pro Asp Gly Ser Tyr Leu Asn Lys Leu Leu
 305 310 315 320
 Ile Ser Arg Ala Arg Gln Asp Asp Ala Gly Met Tyr Ile Cys Leu Gly
 325 330 335
 Ala Asn Thr Met Gly Tyr Ser Phe Arg Ser Ala Phe Leu Thr Val Leu
 340 345 350
 Pro Asp Pro Lys Pro Pro Gly Pro Pro Met Ala Ser Ser Ser Ser Ser

355 360 365
 Thr Ser Leu Pro Trp Pro Val Val Ile Gly Ile Pro Ala Gly Ala Val
 370 375 380
 Phe Ile Leu Gly Thr Val Leu Leu Trp Leu Cys Gln Thr Lys Lys Lys
 385 390 395 400
 Pro Cys Ala Pro Ala Ser Thr Leu Pro Val Pro Gly His Arg Pro Pro
 405 410 415
 Gly Thr Ser Arg Glu Arg Ser Gly Asp Lys Asp Leu Pro Ser Leu Ala
 420 425 430
 Val Gly Ile Cys Glu Glu His Gly Ser Ala Met Ala Pro Gln His Ile
 435 440 445
 Leu Ala Ser Gly Ser Thr Ala Gly Pro Lys Leu Tyr Pro Lys Leu Tyr
 450 455 460
 Thr Asp Val His Thr His Thr His Thr His Thr Cys Thr His Thr Leu
 465 470 475 480
 Ser Cys Gly Gly Gln Gly Ser Ser Thr Pro Ala Cys Pro Leu Ser Val
 485 490 495
 Leu Asn Thr Ala Asn Leu Gln Ala Leu Cys Pro Glu Val Gly Ile Trp
 500 505 510
 Gly Pro Arg Gln Gln Val Gly Arg Ile Glu Asn Asn Gly Gly Arg Val
 515 520 525
 Ser

<210> 32
 <211> 439
 <212> PRT
 <213> Mouse

<400> 32
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 Gly Pro Gly Gly Ser Ser Gly Gly Gln Glu Asp Pro Ala Ser Gln Gln
 35 40 45
 Trp Ala Arg Pro Arg Phe Thr Gln Pro Ser Lys Met Arg Arg Arg Val
 50 55 60
 Ile Ala Arg Pro Val Gly Ser Ser Val Arg Leu Lys Cys Val Ala Ser
 65 70 75 80
 Gly His Pro Arg Pro Asp Ile Met Trp Met Lys Asp Asp Gln Thr Leu
 85 90 95
 Thr His Leu Glu Ala Ser Glu His Arg Lys Lys Lys Trp Thr Leu Ser
 100 105 110
 Leu Lys Asn Leu Lys Pro Glu Asp Ser Gly Lys Tyr Thr Cys Arg Val
 115 120 125
 Ser Asn Lys Ala Gly Ala Ile Asn Ala Thr Tyr Lys Val Asp Val Ile
 130 135 140
 Gln Arg Thr Arg Ser Lys Pro Val Leu Thr Gly Thr His Pro Val Asn
 145 150 155 160
 Thr Thr Val Asp Phe Gly Gly Thr Thr Ser Phe Gln Cys Lys Val Arg
 165 170 175
 Ser Asp Val Lys Pro Val Ile Gln Trp Leu Lys Arg Val Glu Tyr Gly
 180 185 190
 Ser Glu Gly Arg His Asn Ser Thr Ile Asp Val Gly Gly Gln Lys Phe
 195 200 205
 Val Val Leu Pro Thr Gly Asp Val Trp Ser Arg Pro Asp Gly Ser Tyr
 210 215 220
 Leu Asn Lys Leu Leu Ile Ser Arg Ala Arg Gln Asp Asp Ala Gly Met
 225 230 235 240
 Tyr Ile Cys Leu Gly Ala Asn Thr Met Gly Tyr Ser Phe Arg Ser Ala
 245 250 255
 Phe Leu Thr Val Leu Pro Asp Pro Lys Pro Pro Pro Gly Pro Pro Met
 260 265 270
 Ala Ser Ser Ser Ser Ser Thr Ser Leu Pro Trp Pro Val Ile Gly
 275 280 285

Ile Pro Ala Gly Ala Val Phe Ile Leu Gly Thr Val Leu Leu Trp Leu
 290 295 300
 Cys Gln Thr Lys Lys Lys Pro Cys Ala Pro Ala Ser Thr Leu Pro Val
 305 310 315 320
 Pro Gly His Arg Pro Gly Thr Ser Arg Glu Arg Ser Gly Asp Lys
 325 330 335
 Asp Leu Pro Ser Leu Ala Val Gly Ile Cys Glu Glu His Gly Ser Ala
 340 345 350
 Met Ala Pro Gln His Ile Leu Ala Ser Gly Ser Thr Ala Gly Pro Lys
 355 360 365
 Leu Tyr Pro Lys Leu Tyr Thr Asp Val His Thr His Thr His Thr His
 370 375 380
 Thr Cys Thr His Thr Leu Ser Cys Gly Gly Gln Gly Ser Ser Thr Pro
 385 390 395 400
 Ala Cys Pro Leu Ser Val Leu Asn Thr Ala Asn Leu Gln Ala Leu Cys
 405 410 415
 Pro Glu Val Gly Ile Trp Gly Pro Arg Gln Gln Val Gly Arg Ile Glu
 420 425 430
 Asn Asn Gly Gly Arg Val Ser
 435

<210> 33

<211> 322

<212> PRT

<213> Human

<400> 33

Arg Arg Ala Pro Cys Cys Cys Ser Cys Cys Arg Arg Cys Cys Trp Gly
 1 5 10 15
 Pro Ser His Arg Pro Pro Pro Pro Glu Ala Pro Gln Arg Trp Arg Thr
 20 25 30
 Arg Trp Ser His Gly Arg Trp Pro Ala Gly Pro His Cys Ala Ala Ala
 35 40 45
 Val Pro Val Glu Gly Asp Pro Pro Pro Leu Thr Met Trp Thr Lys Asp
 50 55 60
 Gly Arg Thr Ile His Ser Gly Trp Ser Arg Phe Arg Val Leu Pro Gln
 65 70 75 80
 Gly Leu Lys Val Lys Gln Val Glu Arg Glu Asp Ala Gly Val Tyr Val
 85 90 95
 Cys Lys Ala Thr Asn Gly Phe Gly Ser Leu Ser Val Asn Tyr Thr Leu
 100 105 110
 Val Val Leu Asp Asp Ile Ser Pro Gly Lys Glu Ser Leu Gly Pro Asp
 115 120 125
 Ser Ser Ser Gly Gly Gln Glu Asp Pro Ala Ser Gln Gln Trp Ala Arg
 130 135 140
 Pro Arg Phe Thr Gln Pro Ser Lys Met Arg Arg Arg Val Ile Ala Arg
 145 150 155 160
 Pro Val Gly Ser Ser Val Arg Leu Lys Cys Val Ala Ser Gly His Pro
 165 170 175
 Arg Pro Asp Ile Thr Trp Met Lys Asp Asp Gln Ala Leu Thr Arg Pro
 180 185 190
 Glu Ala Ala Glu Pro Arg Lys Lys Lys Trp Thr Leu Ser Leu Lys Asn
 195 200 205
 Leu Arg Pro Glu Asp Ser Gly Lys Tyr Thr Cys Arg Val Ser Asn Arg
 210 215 220
 Ala Gly Ala Ile Asn Ala Thr Tyr Lys Val Asp Val Ile Gln Arg Thr
 225 230 235 240
 Arg Ser Lys Pro Val Leu Thr Gly Thr His Pro Val Asn Thr Thr Val
 245 250 255
 Asp Phe Gly Gly Thr Thr Ser Phe Gln Cys Lys Val Arg Ser Asp Val
 260 265 270
 Lys Pro Val Ile Gln Trp Leu Lys Arg Val Glu Tyr Gly Ala Glu Gly
 275 280 285
 Arg His Asn Ser Thr Ile Asp Val Gly Gly Gln Lys Phe Val Val Leu
 290 295 300
 Pro Thr Gly Asp Val Trp Ser Arg Pro Asp Gly Ser Tyr Leu Asn Lys

305
Pro Leu

310

315

320

<210> 34
<211> 102
<212> PRT
<213> Mouse

<400> 34

Met	Lys	Phe	Leu	Leu	Ile	Ser	Leu	Ala	Leu	Trp	Leu	Gly	Thr	Val	Gly
1			5						10					15	
Thr	Arg	Gly	Thr	Glu	Pro	Glu	Leu	Ser	Glu	Thr	Gln	Arg	Arg	Ser	Leu
			20					25					30		
Gln	Val	Ala	Leu	Glu	Glu	Phe	His	Lys	His	Pro	Pro	Val	Gln	Leu	Ala
		35				40						45			
Phe	Gln	Glu	Ile	Gly	Val	Asp	Arg	Ala	Glu	Glu	Val	Leu	Phe	Ser	Ala
	50					55					60				
Gly	Thr	Phe	Val	Arg	Leu	Glu	Phe	Lys	Leu	Gln	Gln	Thr	Asn	Cys	Pro
65					70					75				80	
Lys	Lys	Asp	Trp	Lys	Lys	Pro	Glu	Cys	Thr	Ile	Lys	Pro	Asn	Gly	Ala
			85						90					95	
Glu	Met	Pro	Gly	Leu	His										
			100												

<210> 35
<211> 147
<212> PRT
<213> Mouse

<400> 35

Met	Lys	Phe	Leu	Leu	Ile	Ser	Leu	Ala	Leu	Trp	Leu	Gly	Thr	Val	Gly
1			5						10					15	
Thr	Arg	Gly	Thr	Glu	Pro	Glu	Leu	Ser	Glu	Thr	Gln	Arg	Arg	Ser	Leu
			20					25					30		
Gln	Val	Ala	Leu	Glu	Glu	Phe	His	Lys	His	Pro	Pro	Val	Gln	Leu	Ala
		35				40						45			
Phe	Gln	Glu	Ile	Gly	Val	Asp	Arg	Ala	Glu	Glu	Val	Leu	Phe	Ser	Ala
	50					55					60				
Gly	Thr	Phe	Val	Arg	Leu	Glu	Phe	Lys	Leu	Gln	Gln	Thr	Asn	Cys	Pro
65					70					75				80	
Lys	Lys	Asp	Trp	Lys	Lys	Pro	Glu	Cys	Thr	Ile	Lys	Pro	Asn	Gly	Arg
			85						90					95	
Arg	Arg	Lys	Cys	Leu	Ala	Cys	Ile	Lys	Met	Asp	Pro	Lys	Gly	Lys	Ile
			100					105					110		
Leu	Gly	Arg	Ile	Val	His	Cys	Pro	Ile	Leu	Lys	Gln	Gly	Pro	Gln	Asp
		115				120						125			
Pro	Gln	Glu	Leu	Gln	Cys	Ile	Lys	Ile	Ala	Gln	Ala	Gly	Glu	Asp	Pro
	130					135					140				
His	Gly	Tyr													
145															

<210> 36
<211> 574
<212> PRT
<213> Mouse

<400> 36

Met	Glu	Ser	Leu	Cys	Gly	Val	Leu	Gly	Phe	Leu	Leu	Leu	Ala	Ala	Gly
1			5						10					15	
Leu	Pro	Leu	Gln	Ala	Ala	Lys	Arg	Phe	Arg	Asp	Val	Leu	Gly	His	Glu
			20					25					30		
Gln	Tyr	Pro	Asn	His	Met	Arg	Glu	His	Asn	Gln	Leu	Arg	Gly	Trp	Ser
		35				40						45			
Ser	Asp	Glu	Asn	Glu	Trp	Asp	Glu	His	Leu	Tyr	Pro	Val	Trp	Arg	Arg
	50					55					60				

Gly Asp Gly Arg Trp Lys Asp Ser Trp Glu Gly Gly Arg Val Gln Ala
 65 70 75 80
 Val Leu Thr Ser Asp Ser Pro Ala Leu Val Gly Ser Asn Ile Thr Phe
 85 90 95
 Val Val Asn Leu Val Phe Pro Arg Cys Gln Lys Glu Asp Ala Asn Gly
 100 105 110
 Asn Ile Val Tyr Glu Lys Asn Cys Arg Asn Asp Leu Gly Leu Thr Ser
 115 120 125
 Asp Leu His Val Tyr Asn Trp Thr Ala Gly Ala Asp Asp Gly Asp Trp
 130 135 140
 Glu Asp Gly Thr Ser Arg Ser Gln His Leu Arg Phe Pro Asp Arg Arg
 145 150 155 160
 Pro Phe Pro Arg Pro His Gly Trp Lys Lys Trp Ser Phe Val Tyr Val
 165 170 175
 Phe His Thr Leu Gly Gln Tyr Phe Gln Lys Leu Gly Arg Cys Ser Ala
 180 185 190
 Arg Val Ser Ile Asn Thr Val Asn Leu Thr Ala Gly Pro Gln Val Met
 195 200 205
 Glu Val Thr Val Phe Arg Arg Tyr Gly Arg Ala Tyr Ile Pro Ile Ser
 210 215 220
 Lys Val Lys Asp Val Tyr Val Ile Thr Asp Gln Ile Pro Val Phe Val
 225 230 235 240
 Thr Met Ser Gln Lys Asn Asp Arg Asn Leu Ser Asp Glu Ile Phe Leu
 245 250 255
 Arg Asp Leu Pro Ile Val Phe Asp Val Leu Ile His Asp Pro Ser His
 260 265 270
 Phe Leu Asn Asp Ser Ala Ile Ser Tyr Lys Trp Asn Phe Gly Asp Asn
 275 280 285
 Thr Gly Leu Phe Val Ser Asn Asn His Thr Leu Asn His Thr Tyr Val
 290 295 300
 Leu Asn Gly Thr Phe Asn Leu Asn Leu Thr Val Gln Thr Ala Val Pro
 305 310 315 320
 Gly Pro Cys Pro Pro Pro Ser Pro Ser Thr Pro Pro Pro Pro Ser Thr
 325 330 335
 Pro Pro Ser Pro Pro Pro Ser Pro Leu Pro Thr Leu Ser Thr Pro Ser
 340 345 350
 Pro Ser Leu Met Pro Thr Gly Tyr Lys Ser Met Glu Leu Ser Asp Ile
 355 360 365
 Ser Asn Glu Asn Cys Arg Ile Asn Arg Tyr Gly Tyr Phe Arg Ala Thr
 370 375 380
 Ile Thr Ile Val Glu Gly Ile Leu Glu Val Ser Ile Met Gln Ile Ala
 385 390 395 400
 Asp Val Pro Met Pro Thr Pro Gln Pro Ala Asn Ser Leu Met Asp Phe
 405 410 415
 Thr Val Thr Cys Lys Gly Ala Thr Pro Met Glu Ala Cys Thr Ile Ile
 420 425 430
 Ser Asp Pro Thr Cys Gln Ile Ala Gln Asn Arg Val Cys Ser Pro Val
 435 440 445
 Ala Val Asp Gly Leu Cys Leu Leu Ser Val Arg Arg Ala Phe Asn Gly
 450 455 460
 Ser Gly Thr Tyr Cys Val Asn Phe Thr Leu Gly Asp Asp Ala Ser Leu
 465 470 475 480
 Ala Leu Thr Ser Thr Leu Ile Ser Ile Pro Gly Lys Asp Pro Asp Ser
 485 490 495
 Pro Leu Arg Ala Val Asn Gly Val Leu Ile Ser Ile Gly Cys Leu Ala
 500 505 510
 Val Leu Val Thr Met Val Thr Ile Leu Leu Tyr Lys Lys His Lys Ala
 515 520 525
 Tyr Lys Pro Ile Gly Asn Cys Pro Arg Asn Thr Val Lys Gly Lys Gly
 530 535 540
 Leu Ser Val Leu Leu Ser His Ala Lys Ala Pro Phe Phe Arg Gly Asp
 545 550 555 560
 Gln Glu Lys Asp Pro Leu Leu Gln Asp Lys Pro Arg Thr Leu
 565 570

<211> 137
 <212> PRT
 <213> Mouse

<400> 37

Ala Glu Ser Arg Leu Ala Ala Pro Arg Ala Pro Pro Ala Ser Leu Leu
 1 5 10 15
 Ala Gly Thr Cys Thr Pro Asn Gln Glu Ala Pro Gly Gly Gly Arg Gly
 20 25 30
 Met Ala Gly Pro Ser Trp Gly Leu Pro Arg Leu Asp Gly Phe Ile Leu
 35 40 45
 Thr Glu Arg Leu Gly Ser Gly Thr Tyr Ala Thr Val Tyr Lys Ala Tyr
 50 55 60
 Ala Lys Lys Asp Thr Arg Glu Val Val Ala Ile Lys Cys Val Ala Lys
 65 70 75 80
 Lys Ser Leu Asn Lys Ala Ser Val Glu Asn Leu Leu Thr Glu Ile Glu
 85 90 95
 Ile Leu Lys Gly Ile Arg His Pro His Ile Val Gln Leu Lys Asp Phe
 100 105 110
 Gln Trp Asp Asn Asp Asn Ile Tyr Leu Ile Met Glu Phe Cys Ala Gly
 115 120 125
 Gly Asp Leu Ser Arg Phe Ile His Thr
 130 135

<210> 38
 <211> 72
 <212> PRT
 <213> Mouse

<400> 38

Thr Val Leu Phe Leu Val Ala Leu Ile Thr Val Gly Met Asn Thr Thr
 1 5 10 15
 Tyr Val Val Ser Cys Pro Lys Glu Phe Glu Lys Pro Gly Ala Cys Pro
 20 25 30
 Lys Pro Ser Pro Glu Ser Val Gly Ile Cys Val Asp Gln Cys Ser Gly
 35 40 45
 Asp Gly Ser Cys Pro Gly Asn Met Lys Cys Cys Ser Asn Ser Cys Gly
 50 55 60
 His Val Cys Lys Thr Pro Val Phe
 65 70

<210> 39
 <211> 1587
 <212> DNA
 <213> Mouse

<400> 39

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 gttggactcc tgggcgtcgt gtggctgctg cgcttgggcc acggcgagga gcggcgggccg
 120
 gagacagcgg cacagcgctg cttctgccag gttagtgggtt acctggacga ctgtacctgt
 180
 gatgtcgaga ccatcgataa gtttaataac tacagacttt tccaagact acaaaagctt
 240
 cttgaaagtg actacttttag atattacaag gtgaacttga agaagccttg tcctttctgg
 300
 aatgacatca accagtgtgg aagaagagac tgtgccgtca aaccctgccca ttctgatgaa
 360
 gttcctgatg gaattaagtc tgcgagctac aagtattctg aggaagccaa ccgcattgaa
 420
 gaatgtgagc aagctgagcg acttgagacc gtggatgagt ctctgagtga ggagacccag
 480
 aaagctgtac ttcaaggac caagcatgat gattcgtcag acagcttctg cgaaattgac
 540
 gatatacagt ccccgatgc tgagtatgtg gacttactcc ttaaccctga gcgctacaca

600
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 660
 aagccacaga caattcaaag gcctttggct tctgggagag gaaaaagtaa agagaacaca
 720
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 780
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 840
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 900
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 960
 agggctctct ccaaagtgtc tccatttttt gagcgtccag attttcagct cttcactggg
 1020
 aataaagttc aggatgcaga aaacaaagcg ttactttctgg agatacttca tgaaatcaag
 1080
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 1140
 aaactaaagg aggacttccg gctacacttt aggaacattt caagaatcat ggactgtgtt
 1200
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 1260
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 1320
 ttccagctaa ccagacaaga aatagtatca ctgtttaatg catttggaag gatttccaca
 1380
 agtgtgagag aactagagaa cttcaggcac ttgttacaga atgttactg aggaggacgg
 1440
 ttggaatgtg cctgtttctg cacaggggaa tttgaagggc aaaatctctt ttagcccat
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 1560
 aaaaaaaaaa aaaaaaaaaa aaaaaaa
 1587

<210> 40
 <211> 2435
 <212> DNA
 <213> Mouse

<400> 40
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 120
 aggtgagagg cggcggcggc ggcgcggctc gggcaccggc cccccagcgg gaggatgaag
 180
 cggcggaacg ccgactgcag taagctccgc cgccccctga agcggaaccg gatcaccgag
 240
 ggtatctacg gcagtacatt tttatacctg aaattcctgg tagtgtgggc acttgtcctc
 300
 cttgccgact ttgtcctgga gttccgattt gaatacctgt ggccgttctg gcttttcac
 360
 agaagcgtct atgattcctt cagataccaa ggactggcct tctcagtatt tttgtttgt
 420
 gtagcattca cttcaaatat catatgtctc ctcttcattc ccatacaatg gcttttttcc
 480
 gctgctagca catatgtatg ggtccagtac gtatggcaca cagaaagggg agtgtgtttg
 540
 cctacagtgt cactctggat cctctttggt tatattgaag cagcaattag atttaaagat
 600
 ctgaaaaact tcatgtaga cctttgtcga ccgtttgctg ctcaactgcat tggataccct
 660
 gtgggtgactt tgggctttgg cttcaaaagt tatgtgagct acaaaatgcg gttaaggaag
 720

780 cagaaggaag ttcagaagga gaacgagttt tacatgcagc ttcttcagca ggccctccct
 840 ccagagcagc aaatgttgca gaagcaggag aaggaggctg aggaagcagc caagggattg
 900 ccggacatgg attcctcgat ccttatacac cacaacggag gcatcccagc caacaaaaaa
 960 ctgtccacaa cgttgccaga gatagaatat cgagaaaaag ggaaagagaa ggacaaggat
 1020 gccaaagaaac acaaccttgg aataaataac aacaacattc tacaacctgt agactctaag
 1080 atacaagaga ttgagtatat ggaaaacat atcaatagta aaagattaaa caatgatctt
 1140 gtgggaagta cagaaaatct cttaaaagag gactcatgca ctgcttcctc aaaaaattac
 1200 aaaaatgcc a gtggagtgt gaactcctcg cctcgaagtc acagcgctac aaatggaagc
 1260 attccttcct cgtctagtaa aaacgagaag aagcagaagt gcaccagcaa gggcccgagt
 1320 gcacacaagg acttaatgga gaactgtatt cctaacaacc agctgagcaa accagacgcg
 1380 ctggtaaggc tggaacaaga cattaanaag ctaaaggctg acctgcaagc cagccggcaa
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 2100 agcataacat acagtgtgc caccagtccc ctgagccccg tgtcccccca ctactcttc
 2160 aagtttgtgg agaccagccc ctctggactt gaccctaattg cctctgtcta ccagcccttg
 2220 aagaagtga ggccaactgt gtgctcgccc aacatttgca accaggaggc ttcgaaaagc
 2280 agcgtctctg gcagtcaaga taaaaaagtt gatattgtgt tttgtgggac tgtatatgtt
 2340 gtcattttta aaggggggaa ataacatcca agtctgatta gaaccgcccc tcagttgttc
 2400 ttggaagttt ttagaagacc tcacggactt tgcagtttat tttgtttggc caacacatta
 2435 aaccattct tggatttcaa gtaaaaaaaa aaaaa

<210> 41
 <211> 1720
 <212> DNA
 <213> Mouse

<400> 41
 gtgacgcgca ggcccaggcg gaagtgcggg cggaggatcc cgagccggat cccgagccgg

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 120
 aaacctgctg cggctgggct cggggctcaa catgtcctgc ctggcgctgt cgggtgctgct
 180
 gctcgcgcag ctgacaggcg ccgccaagaa ttttgaagat gtgagatgta aatgcatctg
 240
 ccctccctat aaagagaatc ctgggcacat ttataataag aatatatctc agaaagattg
 300
 tgattgcctt catgtcgtgg agcccatgcc tgtacgggga cctgatgtag aagcatactg
 360
 tctacgctgt gaatgcaaat acgaagagag aagctctgtc acaatcaagg ttaccattat
 420
 aatttatctc tctattttgg gccttctgct tctgtacatg gtatatctta ccttagttga
 480
 gccatcctg aagaggcgcc tctttggaca ctcccagctg ttgcagagcg atgatgacgt
 540
 tggggatcac cagccttttg caaatgccca tgatgtgctg gcccgctctc gcagccgagc
 600
 caatgttcta aacaagggtg agtacgctca gcagcgctgg aagctccagg tccaggagca
 660
 gcgaaagtct gtcttcgacc gacacgttgt cctcagctaa ctgggaactg gaatcagggtg
 720
 actaggaaga acacgcagac aactgggaag aattgtctgg gtgtccgtgc gttttaatgc
 780
 catgtttgtt ttacaaatc cttgctggat ggaggaagac tccaaactgg aagcaaacc
 840
 catgcttggt attttcctgt taatatatta atagagacat ttttacagca cacagttcca
 900
 agtcaaccag taagtctttt cctacttggt acttttacta ataaaattaa gctgcctgtg
 960
 agttatcttg aagccccgtg cctggaacaa gctctctctt tcttgccaca cagttctaac
 1020
 ttggtgttca agataacttc caggtgtgtt ttgcttctc tttcttggg tgggagagag
 1080
 aggggaaggat gccttgggag tgcttgagta gcttctcaag tgtcttttcc agacagactt
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 1200
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 1320
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 1380
 gctagtttac actgatacct aaacacagtc tcagtgtgtg tggcttctct catcttcttc
 1440
 tagtagctct aaggacttga acatttagaa taaagacatt ttctcttaag cccaagcctc
 1500
 cctggatgat tgacgtacaa atactgatca gccttttctg tcttgctgag aggcagttct
 1560
 ttgaactgat gtgggcagct ttgaacaagg actagagttc agattgcctc tctctgagaa
 1620
 gtctaacagt tattggataa ctggcttttt tcttctaca tctcttttg aatgtaacaa
 1680
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 1720

<210> 42
 <211> 1008
 <212> DNA
 <213> Mouse

<400> 42
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catgggacct ctccaccagt ttctcctgct gctgatcaca gccctgtccc aagccctcaa
 120
 caccacggtg ctgcagggca tggccggcca gtccttgagg gtgtcatgta ottatgacgc
 180
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 300
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 360
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 420
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 480
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 540
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 660
 gggaacacct gtggtcagag ggctggactg tggccaagat gctgggcacc aacttcagat
 720
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 780
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 840
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 900
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 960
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 1008

<210> 43
 <211> 1871
 <212> DNA
 <213> Mouse

<400> 43
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 120
 ccgctccggt tgcaggcgga ggagctgggt gatggctgtg ggcacatagt gacctctcag
 180
 gacagtggca caatgacatc taagaattat ccagggactt accccaatta cactgtgtgt
 240
 gaaaagatca tcacagtccc aaaggggaag agacttattc tgagggtggg agatttgaac
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 360
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 420
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 480
 agcagtgacc atccagatth aataacctgt ttggaacgag gcagccatta tttcgaggaa
 540
 aaatacagca aattctgccc agctggctgt agagacatag cacgagatat ttctgggaat
 600
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 660
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 720
 gaaggactcc tggccaatgg cgtgctctcc oggcatggtt ctttgtcgga aaagcgattt
 780
 ctttttaciaa ccccaggaat gaatattaca actgtggcga ttccatcagt gatcttcac

840
 gccctccttc tgactggaat ggggatcttt gcaatctgta gaaagaggaa aaagaaagga
 900
 aatccatattg tgtcagctga cgctcagaaa acaggctggt ggaagcagat taaatatccc
 960
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 <212> DNA
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Gln	Arg	Cys	Phe	Cys	Gln	Val	Ser	Gly	Tyr	Leu	Asp	Asp	Cys	Thr	Cys
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Asp	Val	Glu	Thr	Ile	Asp	Lys	Phe	Asn	Asn	Tyr	Arg	Leu	Phe	Pro	Arg
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Leu	Gln	Lys	Leu	Leu	Glu	Ser	Asp	Tyr	Phe	Arg	Tyr	Tyr	Lys	Val	Asn
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Leu	Lys	Lys	Pro	Cys	Pro	Phe	Trp	Asn	Asp	Ile	Asn	Gln	Cys	Gly	Arg
				85					90					95	
Arg	Asp	Cys	Ala	Val	Lys	Pro	Cys	His	Ser	Asp	Glu	Val	Pro	Asp	Gly
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Ile	Lys	Ser	Ala	Ser	Tyr	Lys	Tyr	Ser	Glu	Glu	Ala	Asn	Arg	Ile	Glu
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Glu	Cys	Glu	Gln	Ala	Glu	Arg	Leu	Gly	Ala	Val	Asp	Glu	Ser	Leu	Ser
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Glu	Glu	Thr	Gln	Lys	Ala	Val	Leu	Gln	Trp	Thr	Lys	His	Asp	Asp	Ser
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Ser	Asp	Ser	Phe	Cys	Glu	Ile	Asp	Asp	Ile	Gln	Ser	Pro	Asp	Ala	Glu
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Tyr	Val	Asp	Leu	Leu	Leu	Asn	Pro	Glu	Arg	Tyr	Thr	Gly	Tyr	Lys	Gly
			180					185					190		
Pro	Asp	Ala	Trp	Arg	Ile	Trp	Ser	Val	Ile	Tyr	Glu	Glu	Asn	Cys	Phe
		195					200					205			
Lys	Pro	Gln	Thr	Ile	Gln	Arg	Pro	Leu	Ala	Ser	Gly	Arg	Gly	Lys	Ser
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Lys	Glu	Asn	Thr	Phe	Tyr	Asn	Trp	Leu	Glu	Gly	Leu	Cys	Val	Glu	Lys
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Arg	Ala	Phe	Tyr	Arg	Leu	Ile	Ser	Gly	Leu	His	Ala	Ser	Ile	Asn	Val
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His	Leu	Ser	Ala	Arg	Tyr	Leu	Leu	Gln	Asp	Thr	Trp	Leu	Glu	Lys	Lys
			260					265					270		
Trp	Gly	His	Asn	Val	Thr	Glu	Phe	Gln	Gln	Arg	Phe	Asp	Gly	Ile	Leu
		275					280					285			
Thr	Glu	Gly	Glu	Gly	Pro	Arg	Arg	Leu	Arg	Asn	Leu	Tyr	Phe	Leu	Tyr
	290					295					300				
Leu	Ile	Glu	Leu	Arg	Ala	Leu	Ser	Lys	Val	Leu	Pro	Phe	Phe	Glu	Arg
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Pro	Asp	Phe	Gln	Leu	Phe	Thr	Gly	Asn	Lys	Val	Gln	Asp	Ala	Glu	Asn
				325					330					335	
Lys	Ala	Leu	Leu	Glu	Ile	Leu	His	Glu	Ile	Lys	Ser	Phe	Pro	Leu	
		340						345					350		
His	Phe	Asp	Glu	Asn	Ser	Phe	Phe	Ala	Gly	Asp	Lys	Asn	Glu	Ala	His
		355					360					365			
Lys	Leu	Lys	Glu	Asp	Phe	Arg	Leu	His	Phe	Arg	Asn	Ile	Ser	Arg	Ile
	370					375					380				
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Thr	Gln	Gly	Leu	Gly	Thr	Ala	Leu	Lys	Ile	Leu	Phe	Ser	Glu	Lys	Leu
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 <212> PRT
 <213> Mouse

<400> 48

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Lys	Phe	Leu	Val	Val	Trp	Ala	Leu	Val	Leu	Leu	Ala	Asp	Phe	Val	Leu	35	40	45	
Glu	Phe	Arg	Phe	Glu	Tyr	Leu	Trp	Pro	Phe	Trp	Leu	Phe	Ile	Arg	Ser	50	55	60	
Val	Tyr	Asp	Ser	Phe	Arg	Tyr	Gln	Gly	Leu	Ala	Phe	Ser	Val	Phe	Phe	65	70	75	80
Val	Cys	Val	Ala	Phe	Thr	Ser	Asn	Ile	Ile	Cys	Leu	Leu	Phe	Ile	Pro	85	90	95	
Ile	Gln	Trp	Leu	Phe	Phe	Ala	Ala	Ser	Thr	Tyr	Val	Trp	Val	Gln	Tyr	100	105	110	
Val	Trp	His	Thr	Glu	Arg	Gly	Val	Cys	Leu	Pro	Thr	Val	Ser	Leu	Trp	115	120	125	
Ile	Leu	Phe	Val	Tyr	Ile	Glu	Ala	Ala	Ile	Arg	Phe	Lys	Asp	Leu	Lys	130	135	140	
Asn	Phe	His	Val	Asp	Leu	Cys	Arg	Pro	Phe	Ala	Ala	His	Cys	Ile	Gly	145	150	155	160
Tyr	Pro	Val	Val	Thr	Leu	Gly	Phe	Gly	Phe	Lys	Ser	Tyr	Val	Ser	Tyr	165	170	175	
Lys	Met	Arg	Leu	Arg	Lys	Gln	Lys	Glu	Val	Gln	Lys	Glu	Asn	Glu	Phe	180	185	190	
Tyr	Met	Gln	Leu	Leu	Gln	Gln	Ala	Leu	Pro	Pro	Glu	Gln	Met	Leu		195	200	205	
Gln	Lys	Gln	Glu	Lys	Glu	Ala	Glu	Glu	Ala	Ala	Lys	Gly	Leu	Pro	Asp	210	215	220	
Met	Asp	Ser	Ser	Ile	Leu	Ile	His	His	Asn	Gly	Gly	Ile	Pro	Ala	Asn	225	230	235	240
Lys	Lys	Leu	Ser	Thr	Leu	Pro	Glu	Ile	Glu	Tyr	Arg	Glu	Lys	Gly		245	250	255	
Lys	Glu	Lys	Asp	Lys	Asp	Ala	Lys	Lys	His	Asn	Leu	Gly	Ile	Asn	Asn	260	265	270	
Asn	Asn	Ile	Leu	Gln	Pro	Val	Asp	Ser	Lys	Ile	Gln	Glu	Ile	Glu	Tyr	275	280	285	
Met	Glu	Asn	His	Ile	Asn	Ser	Lys	Arg	Leu	Asn	Asn	Asp	Leu	Val	Gly	290	295	300	
Ser	Thr	Glu	Asn	Leu	Leu	Lys	Glu	Asp	Ser	Cys	Thr	Ala	Ser	Ser	Lys	305	310	315	320
Asn	Tyr	Lys	Asn	Ala	Ser	Gly	Val	Val	Asn	Ser	Ser	Pro	Arg	Ser	His	325	330	335	
Ser	Ala	Thr	Asn	Gly	Ser	Ile	Pro	Ser	Ser	Ser	Ser	Lys	Asn	Glu	Lys	340	345	350	
Lys	Gln	Lys	Cys	Thr	Ser	Lys	Gly	Pro	Ser	Ala	His	Lys	Asp	Leu	Met	355	360	365	
Glu	Asn	Cys	Ile	Pro	Asn	Asn	Gln	Leu	Ser	Lys	Pro	Asp	Ala	Leu	Val	370	375	380	
Arg	Leu	Glu	Gln	Asp	Ile	Lys	Lys	Leu	Lys	Ala	Asp	Leu	Gln	Ala	Ser	385	390	395	400
Arg	Gln	Val	Glu	Gln	Glu	Leu	Arg	Ser	Gln	Ile	Ser	Ala	Leu	Ser	Ser	405	410	415	
Thr	Glu	Arg	Gly	Ile	Arg	Ser	Glu	Met	Gly	Gln	Leu	Arg	Gln	Glu	Asn	420	425	430	
Glu	Leu	Leu	Gln	Asn	Lys	Leu	His	Asn	Ala	Val	Gln	Met	Lys	Gln	Lys	435	440	445	
Asp	Lys	Gln	Asn	Ile	Ser	Gln	Leu	Glu	Lys	Lys	Leu	Lys	Ala	Glu	Gln	450	455	460	
Glu	Ala	Arg	Ser	Phe	Val	Glu	Lys	Gln	Leu	Met	Glu	Glu	Lys	Lys	Arg	465	470	475	480

Lys Lys Leu Glu Glu Ala Thr Ala Ala Arg Ala Val Ala Phe Ala Ala
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 Ala Ser Arg Gly Glu Cys Thr Glu Thr Leu Arg Ser Arg Ile Arg Glu
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 Leu Glu Ala Glu Gly Lys Lys Leu Thr Met Asp Met Lys Val Lys Glu
 515 520 525
 Glu Gln Ile Arg Glu Leu Glu Lys Val Gln Glu Leu Arg Lys Tyr
 530 535 540
 Lys Glu Asn Glu Lys Asp Thr Glu Val Leu Met Ser Ala Leu Ser Ala
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 Arg Ile Lys Leu Asp Leu Phe Ser Ala Leu Gly Asp Ala Lys Arg Gln
 580 585 590
 Leu Glu Ile Ala Gln Gly Gln Ile Leu Gln Lys Asp Gln Glu Ile Lys
 595 600 605
 Asp Leu Lys Gln Lys Ile Ala Glu Val Met Ala Val Met Pro Ser Ile
 610 615 620
 Thr Tyr Ser Ala Ala Thr Ser Pro Leu Ser Pro Val Ser Pro His Tyr
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 <212> PRT
 <213> Mouse

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 35 40 45
 Pro Tyr Lys Glu Asn Pro Gly His Ile Tyr Asn Lys Asn Ile Ser Gln
 50 55 60
 Lys Asp Cys Asp Cys Leu His Val Val Glu Pro Met Pro Val Arg Gly
 65 70 75 80
 Pro Asp Val Glu Ala Tyr Cys Leu Arg Cys Glu Cys Lys Tyr Glu Glu
 85 90 95
 Arg Ser Ser Val Thr Ile Lys Val Thr Ile Ile Ile Tyr Leu Ser Ile
 100 105 110
 Leu Gly Leu Leu Leu Leu Tyr Met Val Tyr Leu Thr Leu Val Glu Pro
 115 120 125
 Ile Leu Lys Arg Arg Leu Phe Gly His Ser Gln Leu Leu Gln Ser Asp
 130 135 140
 Asp Asp Val Gly Asp His Gln Pro Phe Ala Asn Ala His Asp Val Leu
 145 150 155 160
 Ala Arg Ser Arg Ser Arg Ala Asn Val Leu Asn Lys Val Glu Tyr Ala
 165 170 175
 Gln Gln Arg Trp Lys Leu Gln Val Gln Glu Gln Arg Lys Ser Val Phe
 180 185 190
 Asp Arg His Val Val Leu Ser
 195

<210> 50
 <211> 227
 <212> PRT
 <213> Mouse

<400> 50
 Met Gly Pro Leu His Gln Phe Leu Leu Leu Leu Ile Thr Ala Leu Ser
 1 5 10 15

Gln Ala Leu Asn Thr Thr Val Leu Gln Gly Met Ala Gly Gln Ser Leu
 20 25 30
 Arg Val Ser Cys Thr Tyr Asp Ala Leu Lys His Trp Gly Arg Arg Lys
 35 40 45
 Ala Trp Cys Arg Gln Leu Gly Glu Glu Gly Pro Cys Gln Arg Val Val
 50 55 60
 Ser Thr His Gly Val Trp Leu Leu Ala Phe Leu Lys Lys Arg Asn Gly
 65 70 75 80
 Ser Thr Val Ile Ala Asp Asp Thr Leu Ala Gly Thr Val Thr Ile Thr
 85 90 95
 Leu Lys Asn Leu Gln Ala Gly Asp Ala Gly Leu Tyr Gln Cys Gln Ser
 100 105 110
 Leu Arg Gly Arg Glu Ala Glu Val Leu Gln Lys Val Leu Val Glu Val
 115 120 125
 Leu Glu Asp Pro Leu Asp Asp Gln Asp Ala Gly Asp Leu Trp Val Pro
 130 135 140
 Glu Glu Ser Ser Ser Phe Glu Gly Ala Gln Val Glu His Ser Thr Ser
 145 150 155 160
 Arg Asn Gln Glu Thr Ser Phe Pro Pro Thr Ser Ile Leu Leu Leu Leu
 165 170 175
 Ala Cys Val Leu Leu Ser Lys Phe Leu Ala Ala Ser Ile Leu Trp Ala
 180 185 190
 Val Ala Arg Gly Arg Gln Lys Pro Gly Thr Pro Val Val Arg Gly Leu
 195 200 205
 Asp Cys Gly Gln Asp Ala Gly His Gln Leu Gln Ile Leu Thr Gly Pro
 210 215 220
 Gly Gly Thr
 225

<210> 51
 <211> 503
 <212> PRT
 <213> Mouse

<400> 51
 Met Gly Thr Gly Ala Gly Gly Pro Ser Val Leu Ala Leu Leu Phe Ala
 1 5 10 15
 Val Cys Ala Pro Leu Arg Leu Gln Ala Glu Glu Leu Gly Asp Gly Cys
 20 25 30
 Gly His Ile Val Thr Ser Gln Asp Ser Gly Thr Met Thr Ser Lys Asn
 35 40 45
 Tyr Pro Gly Thr Tyr Pro Asn Tyr Thr Val Cys Glu Lys Ile Ile Thr
 50 55 60
 Val Pro Lys Gly Lys Arg Leu Ile Leu Arg Leu Gly Asp Leu Asn Ile
 65 70 75 80
 Glu Ser Lys Thr Cys Ala Ser Asp Tyr Leu Leu Phe Ser Ser Ala Thr
 85 90 95
 Asp Gln Tyr Gly Pro Tyr Cys Gly Ser Trp Ala Val Pro Lys Glu Leu
 100 105 110
 Arg Leu Asn Ser Asn Glu Val Thr Val Leu Phe Lys Ser Gly Ser His
 115 120 125
 Ile Ser Gly Arg Gly Phe Leu Leu Thr Tyr Ala Ser Ser Asp His Pro
 130 135 140
 Asp Leu Ile Thr Cys Leu Glu Arg Gly Ser His Tyr Phe Glu Glu Lys
 145 150 155 160
 Tyr Ser Lys Phe Cys Pro Ala Gly Cys Arg Asp Ile Ala Arg Asp Ile
 165 170 175
 Ser Gly Asn Thr Lys Asp Gly Tyr Arg Asp Thr Ser Leu Leu Cys Lys
 180 185 190
 Ala Ala Ile His Ala Gly Ile Ile Thr Asp Glu Leu Gly Gly His Ile
 195 200 205
 Asn Leu Leu Gln Ser Lys Gly Ile Ser His Tyr Glu Gly Leu Leu Ala
 210 215 220
 Asn Gly Val Leu Ser Arg His Gly Ser Leu Ser Glu Lys Arg Phe Leu
 225 230 235 240
 Phe Thr Thr Pro Gly Met Asn Ile Thr Thr Val Ala Ile Pro Ser Val

245 250 255
 Ile Phe Ile Ala Leu Leu Leu Thr Gly Met Gly Ile Phe Ala Ile Cys
 260 265 270
 Arg Lys Arg Lys Lys Lys Gly Asn Pro Tyr Val Ser Ala Asp Ala Gln
 275 280 285
 Lys Thr Gly Cys Trp Lys Gln Ile Lys Tyr Pro Phe Ala Arg His Gln
 290 295 300
 Ser Thr Glu Phe Thr Ile Ser Tyr Asp Asn Glu Lys Glu Met Thr Gln
 305 310 315 320
 Lys Leu Asp Leu Ile Thr Ser Asp Met Ala Asp Tyr Gln Gln Pro Leu
 325 330 335
 Met Ile Gly Thr Gly Thr Val Ala Arg Lys Gly Ser Thr Phe Arg Pro
 340 345 350
 Met Asp Thr Asp Thr Glu Glu Val Arg Val Asn Thr Glu Ala Ser Gly
 355 360 365
 His Tyr Asp Cys Pro His Arg Pro Gly Arg His Glu Tyr Ala Leu Pro
 370 375 380
 Leu Thr His Ser Glu Pro Glu Tyr Ala Thr Pro Ile Val Glu Arg His
 385 390 395 400
 Leu Leu Arg Ala His Thr Phe Ser Thr Gln Ser Gly Tyr Arg Val Pro
 405 410 415
 Gly Pro Arg Pro Thr His Glu His Ser His Ser Ser Gly Gly Phe Pro
 420 425 430
 Pro Ala Thr Gly Ala Thr Gln Val Glu Ser Tyr Gln Arg Pro Ala Ser
 435 440 445
 Pro Lys Pro Val Gly Gly Gly Tyr Asp Lys Pro Ala Ala Ser Ser Phe
 450 455 460
 Leu Asp Ser Arg Asp Pro Ala Ser Gln Ser Gln Met Thr Ser Gly Gly
 465 470 475 480
 Asp Asp Gly Tyr Ser Ala Pro Arg Asn Gly Leu Ala Pro Leu Asn Gln
 485 490 495
 Thr Ala Met Thr Ala Leu Leu
 500

<210> 52
 <211> 757
 <212> PRT
 <213> Mouse

<400> 52
 Met Met Trp Pro Gln Pro Pro Thr Phe Ser Leu Phe Leu Leu Leu Leu
 1 5 10 15
 Leu Ser Gln Ala Pro Ser Ser Arg Pro Gln Ser Ser Gly Thr Lys Lys
 20 25 30
 Leu Arg Leu Val Gly Pro Ala Asp Arg Pro Lys Glu Gly Arg Leu Glu
 35 40 45
 Val Leu His Gln Gly Gln Trp Gly Thr Val Cys Asp Asp Asp Phe Ala
 50 55 60
 Leu Gln Glu Ala Thr Val Ala Cys Arg Gln Leu Gly Phe Glu Ser Ala
 65 70 75 80
 Leu Thr Trp Ala His Ser Ala Lys Tyr Gly Gln Gly Glu Gly Pro Ile
 85 90 95
 Trp Leu Asp Asn Val Arg Cys Leu Gly Thr Glu Lys Thr Leu Asp Gln
 100 105 110
 Cys Gly Ser Asn Gly Trp Gly Ile Ser Asp Cys Arg His Ser Glu Asp
 115 120 125
 Val Gly Val Val Cys His Pro Arg Arg Gln His Gly Tyr His Ser Glu
 130 135 140
 Lys Val Ser Asn Ala Leu Gly Pro Gln Gly Arg Arg Leu Glu Glu Val
 145 150 155 160
 Arg Leu Lys Pro Ile Leu Ala Ser Ala Lys Arg His Ser Pro Val Thr
 165 170 175
 Glu Gly Ala Val Glu Val Arg Tyr Asp Gly His Trp Arg Gln Val Cys
 180 185 190
 Asp Gln Gly Trp Thr Met Asn Asn Ser Arg Val Val Cys Gly Met Leu
 195 200 205

Gly	Phe	Pro	Ser	Gln	Thr	Ser	Val	Asn	Ser	His	Tyr	Tyr	Arg	Lys	Val
	210					215					220				
Trp	Asn	Leu	Lys	Met	Lys	Asp	Pro	Lys	Ser	Arg	Leu	Asn	Ser	Leu	Thr
225					230					235					240
Lys	Lys	Asn	Ser	Phe	Trp	Ile	His	Arg	Val	Asp	Cys	Phe	Gly	Thr	Glu
				245					250					255	
Pro	His	Leu	Ala	Lys	Cys	Gln	Val	Gln	Val	Ala	Pro	Gly	Arg	Gly	Lys
			260					265					270		
Leu	Arg	Ala	Ala	Cys	Pro	Gly	Gly	Met	His	Ala	Val	Val	Ser	Cys	Val
		275					280					285			
Ala	Gly	Pro	His	Phe	Arg	Arg	Gln	Lys	Pro	Lys	Pro	Thr	Arg	Lys	Glu
290						295					300				
Ser	His	Ala	Glu	Glu	Leu	Lys	Val	Arg	Leu	Arg	Ser	Gly	Ala	Gln	Val
305					310					315					320
Gly	Glu	Gly	Arg	Val	Glu	Val	Leu	Met	Asn	Arg	Gln	Trp	Gly	Thr	Val
				325					330					335	
Cys	Asp	His	Arg	Trp	Asn	Leu	Ile	Ser	Ala	Ser	Val	Val	Cys	Arg	Gln
			340					345					350		
Leu	Gly	Phe	Gly	Ser	Ala	Arg	Glu	Ala	Leu	Phe	Gly	Ala	Gln	Leu	Gly
		355					360					365			
Gln	Gly	Leu	Gly	Pro	Ile	His	Leu	Ser	Glu	Val	Arg	Cys	Arg	Gly	Tyr
370						375					380				
Glu	Arg	Thr	Leu	Gly	Asp	Cys	Leu	Ala	Leu	Glu	Gly	Ser	Gln	Asn	Gly
385					390					395					400
Cys	Gln	His	Ala	Asn	Asp	Ala	Ala	Val	Arg	Cys	Asn	Ile	Pro	Asp	Met
				405					410					415	
Gly	Phe	Gln	Asn	Lys	Val	Arg	Leu	Ala	Gly	Gly	Arg	Asn	Ser	Glu	Glu
			420					425					430		
Gly	Val	Val	Glu	Val	Gln	Val	Glu	Val	Asn	Gly	Val	Pro	Arg	Trp	Gly
		435					440					445			
Thr	Val	Cys	Ser	Asp	His	Trp	Gly	Leu	Thr	Glu	Ala	Met	Val	Thr	Cys
450						455					460				
Arg	Gln	Leu	Gly	Leu	Gly	Phe	Ala	Asn	Phe	Ala	Leu	Lys	Asp	Thr	Trp
465					470					475					480
Tyr	Trp	Gln	Gly	Thr	Pro	Glu	Ala	Lys	Glu	Val	Val	Met	Ser	Gly	Val
				485					490					495	
Arg	Cys	Ser	Gly	Thr	Glu	Met	Ala	Leu	Gln	Gln	Cys	Gln	Arg	His	Gly
			500					505					510		
Pro	Val	His	Cys	Ser	His	Gly	Pro	Gly	Arg	Phe	Ser	Ala	Gly	Val	Ala
		515					520					525			
Cys	Met	Asn	Ser	Ala	Pro	Asp	Leu	Val	Met	Asn	Ala	Gln	Leu	Val	Gln
530						535					540				
Glu	Thr	Ala	Tyr	Leu	Glu	Asp	Arg	Pro	Leu	Ser	Met	Leu	Tyr	Cys	Ala
545					550					555					560
His	Glu	Glu	Asn	Cys	Leu	Ser	Lys	Ser	Ala	Asp	His	Met	Asp	Trp	Pro
			565						570					575	
Tyr	Gly	Tyr	Arg	Arg	Leu	Leu	Arg	Phe	Ser	Ser	Gln	Ile	Tyr	Asn	Leu
			580					585					590		
Gly	Arg	Ala	Asp	Phe	Arg	Pro	Lys	Ala	Gly	Arg	His	Ser	Trp	Ile	Trp
		595					600					605			
His	Gln	Cys	His	Arg	His	Tyr	His	Ser	Ile	Glu	Val	Phe	Thr	His	Tyr
610						615					620				
Asp	Leu	Leu	Thr	Leu	Asn	Gly	Ser	Lys	Val	Ala	Glu	Gly	His	Lys	Ala
625					630					635					640
Ser	Phe	Cys	Leu	Glu	Asp	Thr	Asn	Cys	Pro	Ser	Gly	Val	Gln	Arg	Arg
			645						650					655	
Tyr	Ala	Cys	Ala	Asn	Phe	Gly	Glu	Gln	Gly	Val	Ala	Val	Gly	Cys	Trp
			660					665					670		
Asp	Thr	Tyr	Arg	His	Asp	Ile	Asp	Cys	Gln	Trp	Val	Asp	Ile	Thr	Asp
		675					680					685			
Val	Gly	Pro	Gly	Asp	Tyr	Ile	Phe	Gln	Val	Val	Val	Asn	Pro	Thr	Asn
690						695					700				
Asp	Val	Ala	Glu	Ser	Asp	Phe	Ser	Asn	Asn	Met	Ile	Arg	Cys	Arg	Cys
705					710					715					720
Lys	Tyr	Asp	Gly	Gln	Arg	Val	Trp	Leu	His	Asn	Cys	His	Thr	Gly	Asp
				725					730					735	

Ser Tyr Arg Ala Asn Ala Glu Leu Ser Leu Glu Gln Glu Gln Arg Leu
 740 745 750
 Arg Asn Asn Leu Ile
 755

<210> 53
 <211> 169
 <212> PRT
 <213> Mouse

<400> 53
 Met Glu Ala Ala Thr Val Val Leu Ala Leu Ala Leu Leu Gly Ala
 1 5 10 15
 Ala Ala Arg Gly Ala Ala Ser Asp Asp Phe Asn Leu Gly Asp Ala Leu
 20 25 30
 Glu Asp Pro Asn Met Lys Pro Thr Pro Lys Ala Pro Thr Pro Lys Lys
 35 40 45
 Pro Ser Gly Gly Phe Asp Leu Glu Asp Ala Leu Pro Gly Gly Gly Gly
 50 55 60
 Gly Gly Ala Gly Glu Lys Pro Gly Asn Arg Pro Gln Pro Asp Pro Lys
 65 70 75 80
 Pro Pro Arg Pro His Gly Asp Ser Gly Gly Ile Ser Asp Ser Asp Leu
 85 90 95
 Ala Asp Ala Ala Gly Gln Gly Gly Gly Ala Gly Arg Arg Gly Ser Gly
 100 105 110
 Asp Glu Gly Gly His Gly Gly Ala Gly Gly Ala Glu Pro Glu Gly Thr
 115 120 125
 Pro Gln Gly Leu Val Pro Gly Val Val Ala Ala Val Val Ala Ala Val
 130 135 140
 Ala Gly Ala Val Ser Ser Phe Val Ala Tyr Gln Arg Arg Arg Leu Cys
 145 150 155 160
 Phe Arg Glu Gly Gly Ser Ala Pro Val
 165

<210> 54
 <211> 30
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 54
 cccaagctta tgacgcggag ccccgcgctg
 30

<210> 55
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 55
 cgggatccag gccatggcag gcttgtggat gacga
 35

<210> 56
 <211> 37
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 56
ccgctcgagt agatactctt cctccattgt tctcatt
37

<210> 57
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 57
ctgtgcggct caagtgtg
18
